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The American Society of Hospital Pharmacists, an affiliate of the American Pharmaceutical Association, is a national organization devoted to the profession of hospital pharmacy and dedicated to the improvement of pharmaceutical service in the interest of better patient care in hospitals.

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American Society of Hospital Pharmacists

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as the president sees it—

LEO F. GODLEY, *Bronson Methodist Hospital, Kalamazoo, Michigan*

► WE ARE FORTUNATE to be a part of the organization sparked greatly by the enthusiasm and personality of H. A. K. Whitney. Mr. Whitney died last December 15. There are many landmarks in the Hospital Pharmacy landscape that will keep his memory alive.

It seems to be a fairly popular opinion that there is a shortage of pharmacists, though some say this is faulty reasoning in that the shortage is only apparent because there are too many drug stores. President Wayne Campbell of the Michigan State Pharmaceutical Association invited me to participate in a conference to discuss the recruitment of pharmacy students. It was an interesting discussion, though a new area of thinking for me. I am convinced, however, that it is our duty as pharmacists to conduct our own private recruitment programs for this must be one way to help in the perpetuation of our profession.

As far as recruitment goes, we have a job to do in that connection with graduate pharmacists. Certainly, it takes a great deal of well organized thinking to get our message to the type of graduates we want to attract. It is most interesting to note that the number of "positions wanted" ads outnumber "positions open" ads. Whether this is an indication of anything significant is debatable; but I like to think of it as a healthy sign.

I mentioned on this page last month that we had invited the National League of Nursing to participate in our programs related to safety practices and procedures in drug handling in hospitals. Recent correspondence indicates that they have considerable interest in this area of activity and would be interested in establishing a joint effort through their Department of Hospital Nursing to work along these lines. In this connection, the Coordinating Council and the Board of Trustees of the American Hospital Association voted during their last annual meeting "to urge through appropriate channels, that hospital pharmacists extend their responsibilities to include participation in programs dealing with the safe handling of drugs throughout the hospital."

Now that the SOCIETY year is drawing rapidly to a close, I know that many of the affiliated chapters are working very diligently to get their projects and ideas in readiness for the annual meeting. It certainly is important to have these affairs in good form so that the delegates will be able to represent their chapters. You will be getting instructions from Secretary Gloria Francke and Division Director Paul Parker in a very few weeks and I am sure they will want you to ask questions and offer suggestions. I shall be most happy to help in any way I can.

One reason that I know that things are buzzing along enthusiastically is that I have been getting quite a few invitations to meet with affiliated chapters over the country. Michigan, Illinois, North Carolina, Louisiana are a few that I hope to visit in the coming weeks. This is a very enjoyable duty of the President and it is unfortunate that many of these invitations conflict with my calendar. On the other hand, these conflicts may be nature's way of preserving the President for the national convention.

There is a great deal of activity relating to Poison Information Centers among our ranks these days. This activity may possibly be stemming from the National Clearing House for Poison Control Centers of the United States Public Health Service as well as our own Committee headed by Clara Henry. As you know, a pharmacist, Henry L. Verhulst, has been appointed to direct this Clearing House for the Public Health Service. I was fortunate in being able to attend a panel discussion on this subject at the Hospital Pharmacy Section of the Maryland-Delaware-District of Columbia Hospital Association meeting in Washington, D. C. I am mentioning this particularly, because at least one hospital pharmacist that I know of is operating a formal poison information center, and that is Robert Cathcart at Delaware Hospital in Wilmington. Bob is quite enthusiastic about the operation and it is apparently serving a needed function extremely well. Knowing how valuable such a center would be to a hospital and a community, I feel that we, as hospital pharmacists, might use this idea to great advantage.

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News

New A.H.A. Publications

Two new publications of the American Hospital Association are designed to fill gaps in the material available to hospitals and thus to aid hospitals in the provision of good patient care.

The publications are *Hospital Accreditation References* and *Patterns and Principles for Hospital Auxiliaries.*

Hospital Accreditation References provides under one cover for the first time all the official expressions of the Joint Commission on Accreditation of Hospitals, including both previously published statements and unpublished correspondence. Dr. Kenneth B. Babcock, director of the Joint Commission on Accreditation of Hospitals, says in the foreword to the volume, "For some time we at the Joint Commission have seen the need for a comprehensive collection of accreditation literature which might be used as a reference by those seeking specific information about the hospital accreditation program. Accreditation References will, we believe, fill this need and be of great benefit to hospitals and their medical staffs."

Patterns and Principles for Hospital Auxiliaries provides an organized collection of available materials on auxiliaries, including suggestions on principles of procedure and mechanics of operation designed to aid both in the formation of new auxiliaries and in the provision of a guide to established auxiliaries.

Robert A. Hardt Elected Man of the Year

Dr. Robert A. Hardt, Vice President of Hoffmann-La Roche has been elected the retail drug field's Man Of The Year 1957. The award is given annually by *American Druggist* magazine for the most constructive contribution to the drug field. The award was presented to Dr. Hardt on January 9th at a luncheon meeting of the Pharmaceutical Advertising Club of New York City at the Roosevelt Hotel.

The selection is made by a panel of drug industry leaders, including the presidents and secretaries of all national, state, and local pharmaceutical associations and boards of pharmacy, the deans of all accredited colleges of pharmacy, and the editors of all national, sectional, and state drug publications.

Dr. Hardt was named Man Of The Year because of his work as Chairman of the Organizing Committee of the Fourth Pan-American Congress of Pharmacy and Biochemistry, held in Washington, D. C., last November. He is credited with doing a top-notch job of directing and coordinating the vast efforts needed to assure the success of the week-long series of meetings of pharmacists and scientists from 40 nations.

Dr. Hardt heads the Roche Laboratories division of Hoffmann-La Roche, and has served as President of the American Pharmaceutical Manufacturers' Association and of the National Pharmaceutical Council.

► *The International Pharmaceutical Students' Federation* has recently initiated publication of an *IPSF News Bulletin* under the editorship of Professor Glen Moir of the Faculty of Pharmacy, University of British Columbia, Vancouver, B.C.

► *The International Pharmaceutical Students' Federation* is sponsoring a Study Tour to be held in Grenoble, France in mid-August, 1958.

U.S.P. Board of Trustees Holds Annual Meeting

Robert L. Swain and Adley B. Nichols were re-elected Chairman and Secretary, respectively, of the U.S.P. Board of Trustees at the annual Board meeting held at the Pharmacopeia Building in New York City on November 20.

The Board noted the progress being made in the preparation of U.S.P. XVI. Director Miller reported notable activity in every aspect of the revision program, and the first galley proof for the new edition will reach the many proofreaders soon. U.S.P. XVI is scheduled for completion by January 1960.

The Board considered means whereby the American public can be made more fully conscious of the significance of the initials, "U.S.P.," which symbolize the Pharmacopeia and constitute the hallmark of highest standards of purity in drugs. One program favored was that of encouraging more extensive use of the letters, "U.S.P.," where appropriate in advertising and in label copy. The Board noted that this would be the source of greater confidence on the part of the public and thus would be beneficial also to the industry.

Narcotic Addiction

A comprehensive report on narcotic addiction appears in *J.A.M.A. 165*:1707 (Nov. 30), 1834 (Dec. 7), 1968 (Dec.14), 1957. This report, developed by the Council on Mental Health in conjunction with its Committee on Narcotic Addiction on request of the Board of Trustees of the American Medical Association, represents a continuing study of the problems

over a period of two and one-half years. During this time meetings were held with experts in federal agencies responsible for narcotic control, police officials, representatives of the New York Academy of Medicine, a specifically interested member of the American Bar Association, and interested physicians in private practice.

The general feeling of the Council members has been that narcotic addiction should be viewed as an illness and that there should be a progressive movement in the direction of treating addiction medically rather than punitively. It is pointed out in the report that the problem of narcotic addiction in Great Britain is considerably less, percentagewise, than it is in the United States and the associated fact that in Great Britain the approach to the narcotic addict is a much more medically orientated one.

► *The U. S. Public Health Service* has let contracts for $890,000 in hospital, health station and housing improvements for Indians in the Southwest, South Dakota and Nevada. A survey of 970 structures used in providing Indian health services showed many to be in deplorable state of repair and functional efficiency.

Pharmacy Section of A.A.A.S.

Pharmacy Section Np of the American Association for the Advancement of Science held nine sessions December 27 through December 30 at Indianapolis. A total of 26 contributed papers on original studies were reported and one round-table discussion and two symposia were held. Over 200 persons registered as having attended one or more of the Pharmacy Section meetings.

The A.A.A.S. Council, the governing body of the Association, elected Dr. George F. Archambault, Chief of the Pharmacy Branch of the U. S. Public Health Service, a Vice-President of the Association and elected Dr. J. V. Swintosky, of the Smith, Kline and French Laboratories, to serve on the Committee-at-Large of the Section for a four year term. Dr. Archambault will also serve as Chairman of the Section for the coming year.

Of considerable interest, was the symposium on "A Pharmacological Approach to Mental Illness" which attracted interest outside the pharmaceutical group in attendance. Various aspects of the pharmacology of mental illness were discussed by five experts in the field. Dr. J. I. Nurnberger, Chairman of the Department of Psychiatry, Indiana University served as moderator. Dr. I. H. Slater, Head of the Department of Neuropharmacology, Lilly Research Laboratories, discussed the general pharmacological aspects. Dr. T. Verhave, Animal Psychologist at Eli Lilly, discussed animal behavioral studies of drugs used in mental illness. Dr. N. S. Kline, Director of Research at the Rockland State Hospital, discussed clinical studies of the important drugs used in mental illness. Dr. J. Cole, Chief of the Psychopharmacology Service Center of N.I.H. discussed the function and operation of the recently formed center.

Dr. R. C. Anderson, Head of the Toxicology Department of the Eli Lilly Co. and Chairman of the Section, opened the contributed papers sessions which consisted of the presentation of the results of original research. The papers presented were of unusual merit. Dr. G. L. Jenkins and coworkers at Purdue University reported on the synthesis of a series of diphenic acid derivatives. The synthesis of epoxide polymers of steroidal compounds was discussed by Dr. W. F. Head and W. M. Lauter. H. Schriftman, Wyeth Institute, presented a method of analysis of phenylephrine using filter paper chromatography. D. E. Cadwallader from the University of Florida discussed the effect of salts on the permeability of red corpuscles. G. S. Banker and J. E. Christian, Purdue University, presented radioactive tracer techniques for studying the uniformity of distribution of ingredients in tablet matrices. Methods for the measurement of the particle size of powders were reported by Dr. J. V. Swintosky of Smith, Kline and French Laboratories. Gastric and intestinal absorption of penicillin was discussed by R. O. Froman, R. C. Anderson and C. C. Lee, all from the Eli Lilly Laboratories. Dr. O. B. Myres, Butler University, presented information on the gastrointestinal absorption of isoniazid, P.A.B., and promizole. Dr. C. N. Rice, Eli Lilly, discussed the lymphatic absorption of β-sitosterol and cholesterol. The tissue distribution of salicylamide and the oxidation metabolites of salicylates were reported by W. F. Bousquet and J. E. Christian of Purdue University and R. E. Crabtree of Eli Lilly.

The Hospital Pharmacy group had a very informative and well attended full-day session under the direction of Dr. George F. Archambault and Joseph A. Oddis. A number of organizations were represented and participated in the meeting by discussing several important subjects of direct interest to the hospital pharmacist, including legal and other implications in the labeling of nursing station medication containers, local poison control centers, legislative controls over hospital pharmacy at the state level, hospital pharmacy committees, economics and the profession, and several others. A symposium on recent trends in medication

(Continued on Page 103)

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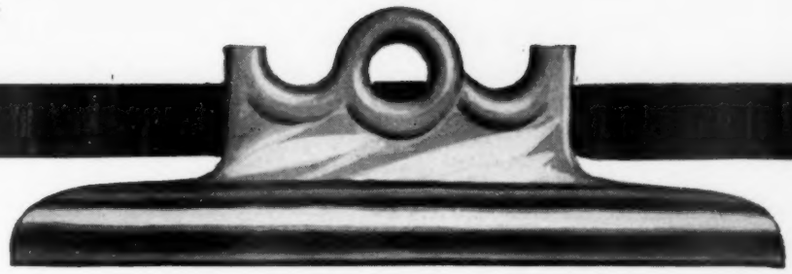

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News

included the following participants: C. J. York spoke on tissue culture; R. H. Behnke spoke on drug therapy in cardiovascular disease; H. D. Bryan presented recent trends in pediatric medication; and Robert C. Bogash discussed the subject of compatibilities of intravenous and intramuscular admixtures. Luncheon, entertainment, and dinner were sponsored by Eli Lilly, Mead Johnson, and McKesson and Robbins, respectively.

On Sunday, December 29, the Pharmacy Section held joint sessions with the Section on the History and Philosophy of Science and the Philosophy of Science Association during which a symposium, "Can Science Provide an Ethical Code?" was held.

Ralph W. Ernsberger, Eli Lilly, presented a paper on how metric advantages can be and have been implemented in pharmaceutical manufacturing. This was followed later by a round-table discussion on the subject moderated by J. T. Johnson, President of the Metric Association. R. J. Dille, R. W. Ernsberger, J. F. Hollings, J. E. Schneider, and R. G. Weigel participated in the discussion.

Eli Lilly and Company sponsored a luncheon and tour of the pharmacological research facilities on Monday afternoon.

Survey of State Pharmacy Laws

The National Drug Trade Conference "Survey of State Pharmacy Laws Relating to the Sale by General Merchants of Non-Prescription Drugs, Variously Designated as 'Patent or Proprietary Medicines,' 'Domestic Remedies,' 'Home Remedies,' 'Household Remedies,' and by Similar Terms," compiled by John M. Seus, B.A., LL.B. has been published.

Copies of this publication are now available from the American Pharmaceutical Association, 2215 Constitution Avenue, N. W., Washington 7, D. C., at $3.00 per copy, including postage.

This Survey is the result of action taken by the National Drug Trade Conference at its annual meetings in 1955 and 1956, based on recommendations of the N.D.T.C. Committee on Uniform State Legislation. This committee recommended that a study be made of all State Pharmacy Laws to determine the present restrictions under these laws with regard to sale of drugs and medicines by general merchants. It was expected that the information thus collected would provide the basis for preparing a proposed uniform statute on this subject.

The subject matter of the publication is divided into three general Chapters and there are 63 Appendices.

The Chapters include:

I. Provisions of State Statutes as to sale of patent or proprietary medicines; sale of home remedies; sale of domestic remedies and similar articles; sale of drugs and/or medicines without restriction; dispensation of drugs and/or medicines in villages and rural areas; powers granted to Boards of Pharmacy in general; powers granted to Boards of Pharmacy to add to or revise lists of drugs and medicines specified in statutes as salable under certain conditions.

II. Power exercised by Boards of Pharmacy in the area of sales of drugs by non-pharmacists.

III. Decisions of the Courts as to definitions of the terms "Patent Medicines," "Proprietary Medicines," "Household and Domestic Remedies"; classification of articles according to restriction of sale; other related matters.

The 63 Appendices cover various tables classifying states as to the provisions of their respective laws regulating the sale of drugs by general merchants, and separate Appendices covering the specific references to the laws in each of the 48 States, the District of Columbia and the Territories of Alaska and Hawaii.

► *Dr. Stuart M. Sessoms* has been appointed Assistant Director of the National Cancer Institute of the National Institutes of Health. Dr. Sessoms has been Assistant Director of the Clinical Center at the National Institutes of Health since early 1954.

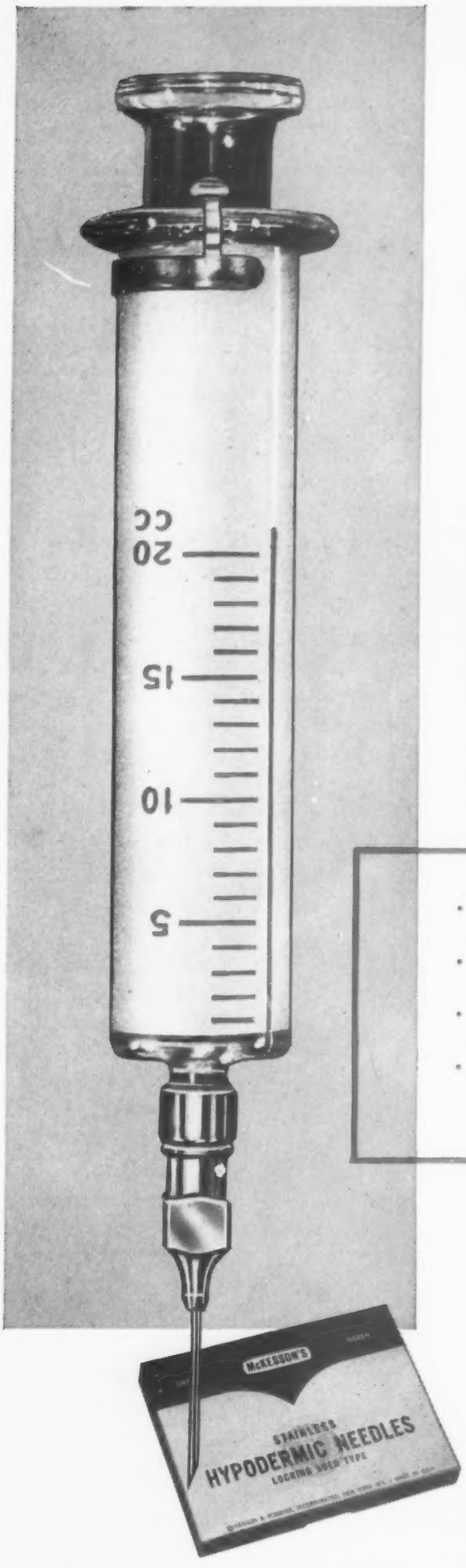
In his new post Dr. Sessoms succeeds Dr. William S. Baum, who has been transferred to the Public Health Service's Division of Indian Health as Assistant Area Medical Officer for Hospital and Medical Care at Phoenix, Arizona.

Dr. Sessoms received a B.S. degree in pharmacy in 1943 at the University of North Carolina, and an M.D. degree in 1946 at the Medical College of Virginia. He served his internship and was a resident in internal medicine at the U. S. Public Health Service Hospital, Baltimore, Maryland, 1947-1950. He was appointed Assistant Chief of Medical Service there where he stayed for two years.

In 1952 and 1953 Dr. Sessoms was assistant resident in medicine at Memorial Center for Cancer and Allied Diseases in New York, following which he joined the National Cancer Institute.

► *All retail pharmacies* should be required by regulation to devote at least 51 percent of their space to drugs, medicines, sickroom supplies and allied products, or be prohibited from calling themselves pharmacies or drug stores, according to a recommendation to the Board of Pharmacy by the Executive Committee of the New York State Pharmaceutical Society.

(Continued on Page 107)



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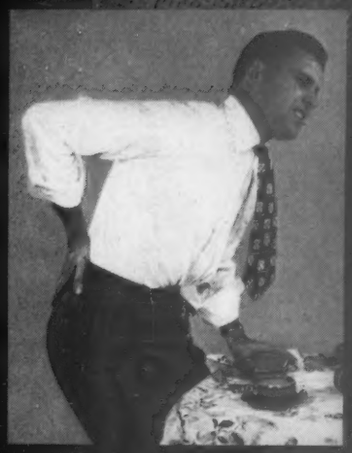

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News

In a statement, the committee asserted that "The primary function of a pharmacy or drug store is to serve the public health." The statement continued: "While we recognize that pharmacists must sell products other than drugs and medicines to survive, as professional members of the public health team, we must place our primary emphasis on service, not economics."

In addition to drugs, medicines and sickroom supplies, products that would be included in the 51 percent of the pharmacy are such things as prosthetic appliances, non-allergenic cosmetics, diabetic foods, dietary supplements, feminine hygiene items, podiatary remedies and appliances, veterinary products, dental needs and baby needs. The area, of course, would also include space occupied by the prescription department of the pharmacy.

A store that did not devote 51 percent of its space to the prescription department and allied drug products would be permitted to use the term "pharmacy" or "drug store" only for that section actually occupied by such products.

► The Joint Committee of the American Hospital Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS will meet in Washington on January 31.

► Institutes sponsored by the American Hospital Association in cooperation with the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS will be held this year in Chicago and Philadelphia. The one at Chicago will be held at the University of Chicago, June 16-20. The second Institute will be held at Temple University in Philadelphia, July 28 - August 2.

► Don Francke, Editor of the AMERICAN JOURNAL OF HOSPITAL PHARMACY, was the principal speaker at the seventy-fifth anniversary banquet of Phi Delta Chi. He discussed the strengths and weaknesses of pharmacy. The banquet was held at the Women's League, University of Michigan, Ann Arbor, on December 28 following the semi-annual convention in Detroit.

► *An Examination of the Concept of Medical Indigence* has been issued by the Health Information Foundation, New York City. This booklet, by Odin W. Anderson, Ph. D. and Harold Alksne, M. A., is the result of a research report conducted to examine the concept of medical indigence in the framework of a medical program financed by public funds—a program designed specifically for people regarded as financially self-sustaining but unable to meet relatively large bills for personal health services.

Canadian Institute on Hospital Pharmacy

The Canadian Society of Hospital Pharmacists will sponsor an Institute on Hospital Pharmacy to be held in Edmonton, Alberta, August 15, 16 and 17, 1958—just prior to the annual convention of the Canadian Pharmaceutical Association.

The outline of the tentative program is as follows:

AUGUST 15

Registration
Orientation and Greetings
Public Relations and the Hospital Pharmacist
Communications and Interdepartmental Relations
  (a) The nurse's viewpoint
  (b) The hospital pharmacist's viewpoint
Pharmacy and Therapeutics Committee and the Formulary System
Pharmacy and Therapeutics Committee in Action

A Formulary or a Basic Drug List?
Preparation of a Formulary or Drug List
New Drugs and Drug Therapy
Economies of Ward Stock Preparations
  (a) Viewpoint of a government hospital pharmacist
  (b) Viewpoint of a 'civilian' hospital pharmacist
Saskatchewan Regional Hospital Set-up
Workshop (Appropriate topics to be assigned to each group divided as follows: (a) DVA & Armed Services, (b) Pharmacists in small hospitals under 150 beds, (c) Pharmacists in hospitals from 150-300 beds, (d) Pharmacists in hospitals 300 beds and over.
Review of Workshops

AUGUST 16

Official Breakfast
Radioactive Isotopes
Dermatological Preparations
Formulation and Product Development (Panel)
Research and Hospital Pharmacists

Manufacturing (Panel and Demonstration)
Writing for Publication
Information Sources
Pharmacy Services in Small Hospitals (Panel)
Dinner

Open Forum

AUGUST 17

Pharmacy Services in Government Hospitals
Handling of 'Emergency' Medications (Panel)
Legal Aspects of Professional Practice in the Hospital:
  (a) Liability of the Hospital
  (b) Liability of the Hospital Pharmacist
Central Supply and the Pharmacy (Two points of view)
Clinic Session
Clinic Session Reports

Dinner and Presentation of Certificates
C.S.H.P. Annual Meeting

► Basil Ketcham, Chief of Pharmaceutical Services at the Veterans Administration Hospital in Philadelphia, played an active role in the Phi Delta Chi Convention held in Detroit, December 27 and 28. He is editor of *The Communicator*, a publication of Phi Delta Chi.

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*U.S. Pat. 2581850; 2506294

1. Dripps, R.C.: Hazards of the Immediate Postoperative Period, J.A.M.A. 7:795 (Oct. 19, 1957). [This reference reviews postoperative hazards, and does not refer to Adrenosem Salicylate].

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News

► The 1958 Annual Convention of the American Hospital Association will be held in Chicago, August 18-21.

Frazier To Receive Whitney Award

Walter M. Frazier

Walter M. Frazier of Springfield, Ohio has been named the 1958 recipient of the Harvey A. K. Whitney Lecture Award for his outstanding contributions to American hospital pharmacy.

The award was established by the Michigan Society of Hospital Pharmacists in 1950 to honor Harvey A. K. Whitney, who was a hospital pharmacy leader and a founder of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. This award is especially significant this year due to the recent death of Mr. Whitney.

A native of southern Ohio, Mr. Frazier is a graduate of the Cincinnati College of Pharmacy. He has served as Chief Pharmacist at Springfield City Hospital since 1938, where he has developed a model pharmacy department. He is a charter member of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. As President of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS during the SOCIETY'S Decennial Meet held in Philadelphia in 1952, he was instrumental in organizing one of the most outstanding meetings ever held by the group. He was also one of the early secretaries of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS and has been a member of the Executive Committee for several years. He is currently a member of the Joint Committee of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS and the American Hospital Association and has served on the Policy Committee of the Division of Hospital Pharmacy of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. His efforts and leadership have contributed greatly to the improvement of pharmaceutical services in hospitals throughout the nation.

This award presentation will highlight a testimonial dinner scheduled for Monday evening, April 21, 1958 in Los Angeles, California. This event is being held in conjunction with the Annual Meeting of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS and the Convention of the American Pharmaceutical Association.

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for ECONOMY

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Requires less frequent irrigating post-operatively.

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†Schulte, et al., "Clinical Use of Cytal in Urology," Jrnl. of Urology, May 1954.

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[1]Slanetz, L.W.: J. Dent. Res. 31:35. 1952.

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Rhode Island Society

Members of the Rhode Island Society of Hospital Pharmacists met at the McKesson and Robbins meeting room in Providence on November 12 at 7:30 P.M. President Edward Gilberti opened the meeting with a discussion concerned with problems facing the local hospital pharmacists and responsibility of the chapter for seeking methods of improving service in hospitals. He also emphasized the need for participation in the national organizations. Further discussion by the members led to recommendations for re-organization of the meetings during the new year and it was suggested that they follow an educational theme. Also, meetings will be held following a group dinner at 6:30 in the evening. It is anticipated that more members will be able to participate under this plan.

A letter from the national organization asking for suggestions with regard to revising the Minimum Standard for Pharmacies in Hospitals was read. It was suggested that the individual members review the Standard and that the Program Committee plan a panel discussion for the January meeting.

During the business session the following new officers were elected to serve during the coming year: *President,* Joseph Giardino, Roger Williams General Hospital; *Vice-President,* Frank E. Chase, Lying-In-Hospital, *Secretary,* Norman R. Caron, St. Luke's Hospital; and *Treasurer,* Joseph Mercurio, St. Joseph's Hospital, all in Providence.

Arizona Society

Mr. Al Duncan, Secretary of the Arizona State Board of Pharmacy, was the principal speaker at the November meeting of the Arizona Society of Hospital Pharmacists. The meeting was held at the State Hospital in Phoenix. In Mr. Duncan's discussion, he covered the present laws and regulations affecting hospital pharmacy practice in the State, pointing out that the laws are not always adequate but that the responsibility for proper maintenance of ethical and practical standards falls upon the individual. On conclusion of the discussion, Mr. Eli Schlossberg proposed that a committee of the Arizona Society of Hospital Pharmacists be appointed to meet with members of the Arizona State Board of Pharmacy to discuss laws and regulations affecting pharmacy practice in hospitals in Arizona.

During the business session the following subjects were covered: plans for a program in conjunction with the Convention of the Arizona Pharmaceutical Association which will be held in Tucson, April 12, 13, and 14; the distribution and handling of drugs in rest homes in the State; and a report on the efficacy of certain combinations of antibiotics.

Members of the Arizona Society are slated to meet on January 19 at St. Mary's Hospital in Tucson, Arizona.

Southeastern New York State Chapter

The December meeting of the Southeastern New York State Chapter of the American Society of Hospital Pharmacists was held at Lenox Hill Hospital in New York City with President Harold Neham presiding. Due to a small attendance which resulted from the Subway strike, the business session was postponed.

Included on the Program was a discussion on "The Pharmacist, The Physician, and The Law," by Mr. William Feeney, of the Key Pharmaceutical Company. At the conclusion of the formal presentation, the speaker answered questions relating to the laws and their application to hospital pharmacy practice. Points of particular interest were malpractice and contributory negligence.

Northeastern New York Society

The regular monthly meeting of the Northeastern New York Society of Hospital Pharmacists was held on Wednesday, December 4, 1957, at St. Peter's Hospital in Albany at 8:00 P.M. There were twenty members present. After the reports of the officers and various committee chairmen, the group conducted a panel discussion on "Narcotic Procedures in Various Hospitals." Members of the panel included Lucy Manvel, Chief Pharmacist, Leonard Hospital, Troy; Fay Peck, Jr., Assistant Pharmacist-in-Chief, Albany Hospital, Albany; and Benjamin Teplitsky, Chief, Pharmacy Service, Veterans Administration Hospital, Albany. Cal Frank J. Smith, Chief of the Narcotic Control Section for the State of New York also spoke. The panel was followed by a general discussion by the group members. A buffet followed the meeting.

The meeting for December was the Annual Christmas Dinner which was held in the Sheraton-Ten Eyck Hotel in Albany on Wednesday, December 18, 1957. After dinner, the fifty-two members and guests enjoyed a presentation of Lee J. Hymel, Assistant Sales Manager, Wyeth Laboratories. He spoke on the "Future Growth of Hospital Pharmacy."

Texas Society

Officers elect of the Texas Society of Hospital Pharmacists to serve during 1958 include *President,* James D. McKinley, Jr., M. D. Anderson Hospital, Houston; *Vice-President,* William T. Clarke, Jr., V. A. Hospital, Waco; *Secretary,* Susan Campbell, Baptist Memorial Hospital, Beaumont; and *Treasurer,* Blanche Groos, San Antonio State Hospital, San Antonio.

The new officers will be installed at a business meeting of the Texas Society on Sunday, February 16, at a meeting which will be held in conjunction with the Annual Seminar in Austin.

Indiana Chapter

For the third quarterly meeting of the Indiana Chapter of the American Society of Hospital Pharmacists, the State was divided into three areas, making it possible for more pharmacists to attend the meetings. The northern area meeting was held on October 26 at the Elkhart General Hospital in Elkhart, with Eileen Foley, Frank Duncan, and William Wissman presiding. The central area meeting was held at the new Community Hospital in Indianapolis on October 26, with Kenneth Gillmore and Mildred Wiese presiding. Information on the third area meeting is not available.

The meetings scheduled for the two areas followed somewhat the same pattern with a tour of the hospitals and round table discussions covering subjects of particular interest to those in attendance.

Florida Society of Hospital Pharmacists

The Florida Society of Hospital Pharmacists recently held a meeting in connection with the annual convention of the Florida Hospital Association. A feature of the hospital pharmacy program was a talk on "Establishing and Supervising an Outpatient Clinic Pharmacy," by Mrs. Virginia Yearick, who is president of the Dade County Society of Hospital Pharmacists.

Officers for the coming year, who were elected at the meeting, are Mr. Carl Dell, *President;* and Miss Jean Whitmore, *Secretary.*

Alabama Society

Members of the Alabama Society of Hospital Pharmacists met at the Veterans Administration Hospital in Birmingham, Alabama on October 12 and 13. Following registration and a noon luncheon on Saturday, the group heard papers on "Physiology and Pharmacology of Adrenal Cortex Glands," by Dr. S. R. Hill and "Uses and Limitation of Tranquilizing Drugs in Psychiatry," by Dr. Henry Spira. A dinner and social evening was held on Saturday evening. The meeting reconvened on Sunday morning for a business session during which time new officers were elected including *President,* Jack Cole; *Vice-President,* Bill Adams; and *Secretary-Treasurer,* Earl Cobb.

A special committee was appointed to study the Alabama pharmacy laws with regard to hospital pharmacy. Also during the business session, Mr. Edward Whiddon was appointed to serve as a panel member at the January meeting of the Alabama Pharmaceutical Association. The panel will cover "Hospital Pharmacists Contribution to Better Patient Care."

At the close of the meeting Miss Mary Lancaster, who has served as President during the past year, presented the Society with an engraved gavel and turned the meeting over to the new President, Mr. Jack Cole. Committee appointments for the coming year were made.

Southern California Society

Joseph H. Beckerman, Assistant Chief Pharmacist, University of California Hospital, Los Angeles, was recently elected president of the Southern California Society of Hospital Pharmacists. Other officers for the coming year include *Vice-President,* John H. Plake, White Memorial Hospital; *Recording Secretary,* Ethel Kopple, Crenshaw Hospital; and *Treasurer,* Wendell Hill, Orange County Hospital. The election took place at the November meeting of the Southern California Society held at the Queen of Angels Hospital in Los Angeles.

New officers of the Southern California Society of Hospital Pharmacists. Shown left to right: Joseph H. Beckerman, Ethel Kopple, Wendell Hill and John Plake

Sister Marietta, Director of Nurses, Queen of Angels Hospital, greeted the group and welcomed them on behalf of Sister Junilla. Ernest Kelso, Vice-President, opened the meeting by introducing Joseph Beckerman who presented the speakers featured on the program.

Dr. James Cremin, Pathologist at Queen of Angels Hospital, gave an interesting talk on "Blood, Blood Products and Their Uses." The Executive Secretary of the California State Board of Pharmacy, Floyd Heffron, spoke on recent regulations and activities of the Board and its Inspectors, chiefly in respect to hospitals and small institutions where drugs are administered.

Burnell H. Blanchard, Chief Inspector, Bureau of Narcotic Enforcement, Los Angeles, gave some interpretations of the new narcotic regulations. Charles Towne, who recently returned from Washington, D.C. where he attended the Pan-American Congress on Pharmacy and Biochemistry, reported on the meetings and business sessions held by the various groups participating in the Congress. He also summarized preliminary plans for the A.Ph.A. Convention to be held in Los Angeles next April.

Northern California Society

The one hundred ninth meeting of the Northern California Society of Hospital Pharmacists was held on November 12 at Highland-Alameda County Hospital in Oakland. Mr. Clarence Richard of the Upjohn Company was introduced by Program Chairman Al Seubert. Mr. Richards showed the film entitled "Borderlines of Cancer."

During the business session results of the election of officers for 1958 were announced as follows: *President,* Mathilde Herby; *Vice-President,* Jessie Lavender; *Secretary,* Molly Chin; and *Treasurer,* Charles Jackson.

A summary report on the Pfizer Seminar which was held on October 19 was presented by Mr. Charles Bertrand. It was noted that the Seminar was a success with eighty-five registrants. Tentative plans were outlined for a similar type meeting during the coming year.

Announcements were made regarding plans for future meetings including the Association of Western Hospitals Convention which will be held in San Francisco in April. Mrs. Marie Kuck has been named Chairman of the Hospital Pharmacy Section and Al Seubert will act as Secretary.

New members introduced at the November meeting of the Northern California Society included Edward E. Madden, Jr. of the U.S. Public Health Service hospital in San Francisco; Masao Fujii of Brookside Hospital in San Pablo; and Julius Nasatir of San Luis Obispo County General Hospital in San Luis Obispo.

Western Pennsylvania Society

The greatest problem in the treatment of epilepsy today is social acceptance of the patient, as diagnostic procedures and drugs have done much to recognize and control most cases. This was the theme of the film "The Medical Treatment and Social Problems of Epilepsy," shown by Dr. Elmo Masucci, Veterans Administration Hospital, Leech Farm Road, Pittsburgh, at the November 21 meeting of the Western Pennsylvania Society of Hospital Pharmacists, held at Mercy Hospital, Pittsburgh.

At the business meeting following the program, special projects of the Society were discussed. Current projects include a drive to increase membership in the local and national Societies, and a survey of hospital pharmacy inventories. Everyone seemed interested in the newest proposal—an exchange of pharmacy interns among the member hospitals.

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1. Hunter, J.A., et al.: Hospital Management *83*:86 (March) 1957.

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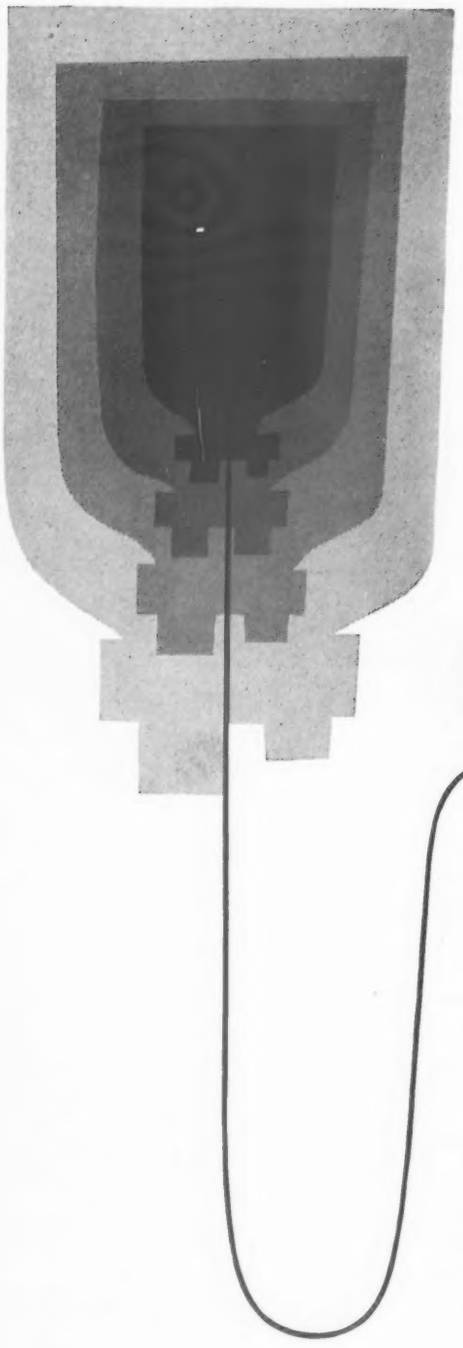

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Dear Sirs:

Appreciation for Law Issue

DEAR SIRS: A word of appreciation to Dr. Archambault on behalf of the Greater New York Chapter of the American Society of Hospital Pharmacists for the splendid job he did in his recent article on "The Law of Hospital Pharmacy," which appeared in the May-June edition of *The Bulletin.*

SISTER MARY VIRGINIA, *President*
Greater N. Y. Chapter of the ASHP
Mercy Hospital
Rockville Centre, L.I., New York

Interest in Editorial

DEAR SIRS: I'm impressed with your editorial [Ten Guides for the Operation of a Formulary System] on page 663 of *The Bulletin* for November-December, and it seems to me that these are principles which have meaning for administrators as well as pharmacists.

I wonder, therefore, if we can have your permission to reprint this in *The Modern Hospital* . . . with appropriate credit to you and to *The Bulletin.*

ROBERT M. CUNNINGHAM, JR., *Editor*
The Modern Hospital
919 N. Michigan Ave.
Chicago 11, Illinois

Interested in Internship

DEAR SIRS: I am a pharmacist who has graduated this year from the School of Chemistry and Pharmacy of the University of Antioquia, Medellin-Colombia, and I would like to come to the United States to practice for awhile. I want to know if it is possible to arrange for an internship in hospital pharmacy in one of the hospitals of the United States.

If you need information as to my qualifications, etc., I will be glad to send it to you right away.

DR. SALOMON KURZER
Calle 65 No. 50D-51
Medellin-Colombia-S.A.

Exchange of Publications

DEAR SIRS: We would like to establish a regular exchange between *Bibliografica Farmaceutica* and *The Bulletin of the American Society of Hospital Pharmacists.*

We hope you will agree to this exchange of publications and wish to thank you for your cooperation.

G. MURALLI, *Editor*
Bibliografica Farmaceutica
Milano, Italia

DEAR SIRS: The Editorial Office of the military medical review *Vojnosanitetski Pregled* has the honour to inform you that in the future the review will be published twice yearly in foreign languages—English, French and Russian. Our review deals with articles in all fields of general and military medicine and pharmacy and in this new publication will be published selected outstanding articles which have appeared during the year.

Our intention is to facilitate thereby a better exchange of experiences and points of view within all fields of general and military medicine and pharmacy and to establish a closer contact and cooperation with other medical reviews on an international level.

Please be so kind and let us know if you are interested in receiving a specimen copy and if you would like to cooperate with us in exchanging publications.

COLONEL DR. IVAN PAVLETIC,
Editor in Chief
Review of Military Medicine and Pharmacy of the Yugoslav National Army
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Nemanjina 15, Beograd
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DEAR SIRS: We would like to establish a regular exchange of your journal *The Bulletin of the American Society of Hospital Pharmacists* for one or two journals of your choice from the attached list.

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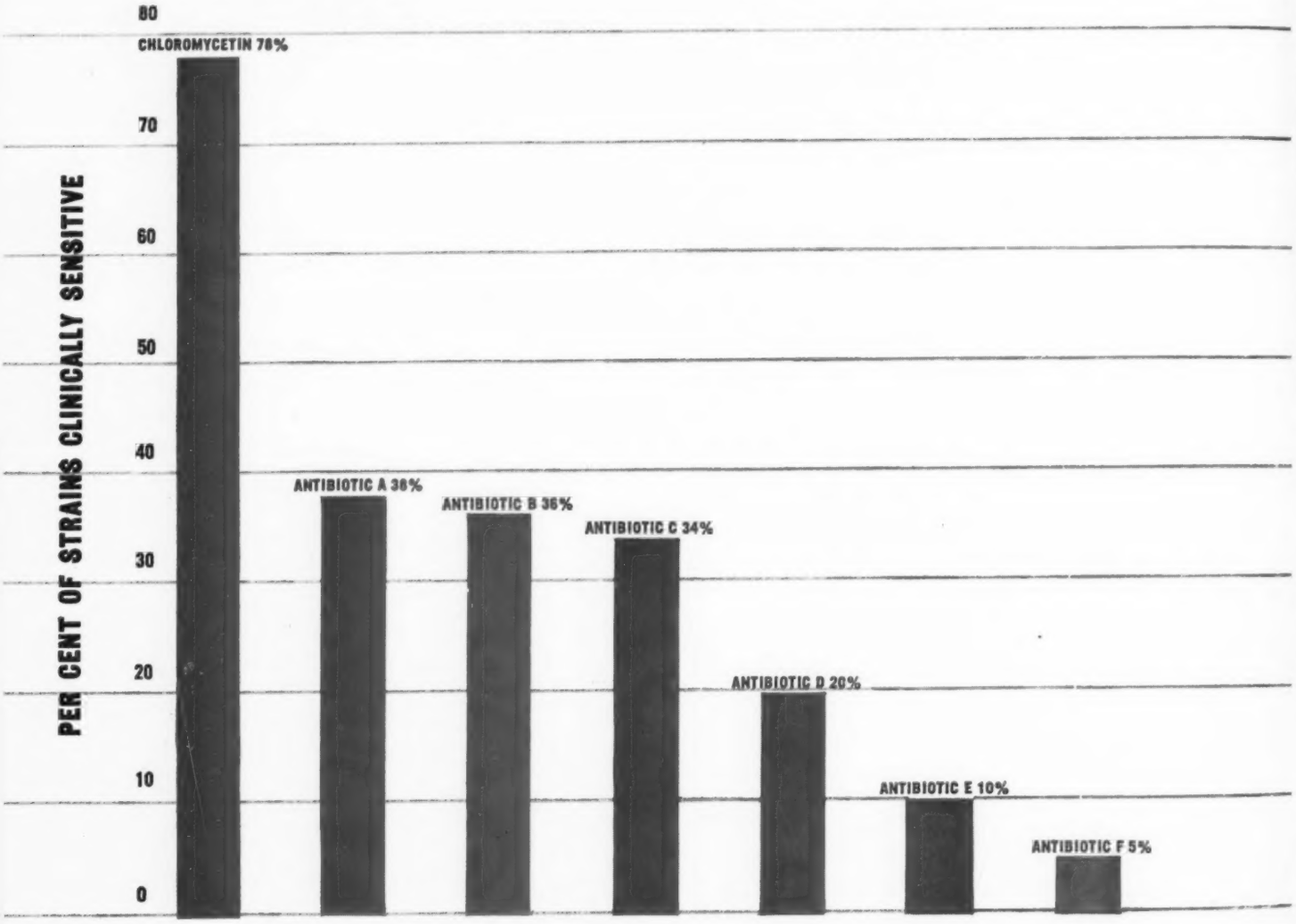

COMPARATIVE SENSITIVITY OF MIXED PROTEUS SPECIES TO CHLOROMYCETIN AND SIX OTHER WIDELY USED ANTIBIOTIC AGENTS*

*This graph is adapted from Waisbren, B. A., & Strelitzer, C. L.: *Arch. Int. Med.* 99:744, 1957. It represents *in vitro* data obtained with strains isolated from patients between the years 1951 and 1956. Inhibitory concentrations, ranging from 3 to 25 mcg. per ml., were selected on the basis of usual clinical sensitivity.

CHLOROMYCETIN (chloramphenicol, Parke-Davis) is a potent therapeutic agent and, because certain blood dyscrasias have been associated with its administration, it should not be used indiscriminately or for minor infections. Furthermore, as with certain other drugs, adequate blood studies should be made when the patient requires prolonged or intermittent therapy.

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by DON E. FRANCKE

Need for Trained Hospital Pharmacists

► ONE OF THE BASIC RESPONSIBILITIES of a professional society is to plan soundly for the future. In the pages of this issue of the JOURNAL, Dr. George F. Archambault has presented data showing the need for an increased number of trained hospital pharmacists. His conservative estimates indicate that, beginning in 1960, there will be an annual need for more than 400 additional hospital pharmacists and by 1970 these requirements will rise to more than 470 annually. It should be emphasized that Dr. Archambault's predictions are conservative. Certainly, the SOCIETY must heed the need for trained practitioners and prepare to fill it.

The basis of progress in hospital pharmacy, as in other professions, is availability of well-trained practitioners. This implies practitioners with a good educational background who have an opportunity for a well-planned program of specialized training in hospital pharmacy. The education of practitioners is the responsibility primarily of the colleges of pharmacy. On the other hand, pharmacists themselves have a responsibility in education. Theirs is the responsibility of informing those in education of their needs, of setting imaginative educational goals for their specialty, of influencing practitioners and educators to accept these goals, and of persistently presenting their ideas until they are adopted or an acceptable compromise plan developed. Practitioners also have a responsibility for the continuous after-graduation education and training of their members. In this field the SOCIETY, with the American Pharmaceutical Association and the American and Catholic Hospital Associations, has shown commendable and outstanding leadership through the development of several annual institutes on hospital pharmacy conducted on a national basis, and numerous seminars conducted on a local and regional basis.

But it is the training of future hospital pharmacists which is the particular responsibility of practitioners. One of the accepted hallmarks of each profession is that its members provide training to future practitioners. At the SOCIETY's very first meeting in Columbus, Ohio in 1943, plans were laid for establishing standards for hospital pharmacy internships. During the course of several years, the Minimum Standard for Pharmacy Internships in Hospitals was drafted, widely circulated, fully discussed and, in 1949, adopted by the SOCIETY. Since that time several revisions have been accepted in an effort to strengthen the training offered to future practitioners.

Throughout these years one of the greatest voids in the upgrading of internship programs has been the lack of an accreditation program. Responsibility for accrediting hospital pharmacy internship programs was assigned by the SOCIETY to the Division of Hospital Pharmacy in 1951. Since that time a great deal of necessary planning has been done and some unofficial inspections have been made, but lack of funds has made it impossible to launch a full-scale accreditation program.

However, the stage has now been set for an accreditation program by the Division of Hospital Pharmacy. This is made possible through funds made available by Lederle Laboratories as a grant to the SOCIETY, which has allocated money to the Division of Hospital Pharmacy for accreditation purposes. Thus, this important task so vital to meeting the needs of well-trained hospital pharmacists should soon be under full sail.

There are several areas in which practicing hospital pharmacists can contribute to meeting the need for trained hospital pharmacists. They can, by individual and group action, influence the better students to select hospital pharmacy as a career. A splendid example of group action is the work of the Akron Society of Hospital Pharmacists in inviting annually large numbers of pharmacy students to a well-planned orientation meeting and providing conducted tours of hospital pharmacies in the Akron Area. Second, hospital pharmacists can offer formal, well-planned and meaningful internship training programs for which there is a great need. And hospital pharmacists can make their specialty more attractive to future practitioners by striving constantly to improve pharmacy as a professional service within their hospitals, by making the practice of hospital pharmacy an even more satisfying professional experience for practitioners, and by increasing the remuneration of hospital pharmacists to a level which will attract and retain capable newcomers to the field.

moniasis of nails

SKIN TESTING MATERIALS

for the diagnosis of disease

by EDWARD F. CROUMEY and M. LINDSAY MITCHELL

► THE HUMAN BEING IS KNOWN TO ACQUIRE a hypersensitivity to various agents and, as a result to develop such allergy diseases as allergic rhinitis, drug allergy and contact dermatitis. He may become sensitive to the allergic products of the fungi, bacteria, parasites, and viruses. It is on this principle that the use of skin testing antigens is based.

The physician is trained in the diagnosis and treatment of these diseases. It is the function of the pharmacist to prepare or locate the various aids the physician requires in the practice of his profession.

It is not the purpose of this paper to describe extensively the result or to evaluate the efficiency of the tests; but merely to make known the availability of the tools so essential for the diagnosis of disease. The skin testing materials mentioned in this paper are a partial listing of the aids the physician has available for use in the differential diagnosis of these diseases.

General Discussion

The appropriate antigen solution generally is prepared using bodies or extracted products of bacteria, viruses, parasites, or fungi. The amount, usually 0.1 ml., is injected into the skin. It is important that the material be injected into, and not beneath the skin. A short (½″) 24 or 25 gauge needle is used with the bevel up and the shaft almost parallel to the skin. The needle point and bevel must be short. In all skin test procedures it is desirable to establish control by making a simultaneous inoculation in a comparable area of skin using inactivated whole antigen or the diluent in which the antigen was prepared. In this way, nonspecific reactions may be detected. Fewer false reactions occur when injections are made several inches below the elbow.

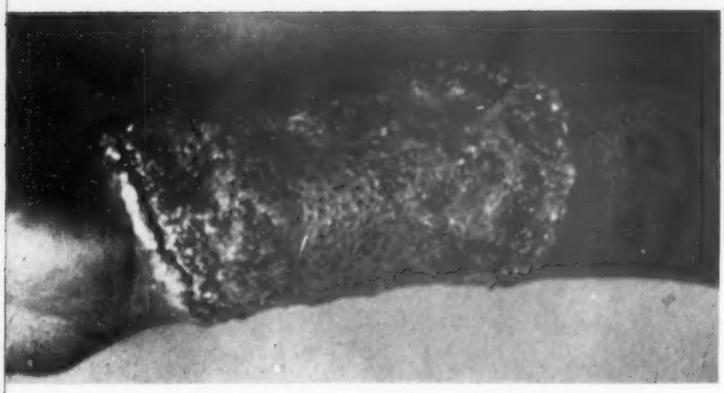
It is well to remember that sensitivity, once established, may persist for years or even for the life of the patient. Therefore, a positive reaction means only that the patient has at some time encountered the particular infectious agent and has developed a sensitivity toward that particular agent. A distinction between previous infection and a current infection cannot be made by skin testing unless one has the opportunity to observe a negative reaction which subsequently is positive after development of clinical signs or symptoms of the disease.

Negative tests do not prove with certainty the absence of disease. Positive tests may be attributable to tuberculosis sensitization and penicillin sensitivity. When a specific test is positive while all other tests are negative, however, it may be presumed that a disease infection corresponding to the test is involved.

Skin testing antigens are not completely free from side effects. The usual reactions are: (1) local irritation and possible necrosis of the tissues; (2) focal reactions with resulting spread of preëxisting lesions; and (3) systemic reactions, characterized by fever and malaise, with occasional leucocytosis. The careful standardization of antigen material as well as the use of high dilutions will help to minimize the danger of side effects.

Separate syringes, appropriately marked to avoid exchange, must be reserved for each individual test to avoid false results due to the adherence of the antigen to the syringe barrel.

EDWARD F. CROUMEY is Chief Pharmacist and M. LINDSAY MITCHELL is Assistant Chief Pharmacist at The Mary Fletcher Hospital, Burlington, Vt.



blastomycosis

Skin Tests for Fungus Diseases

Blastomycosis

Synonyms. Blastomycetic dermatitis, saccharomycosis, Gilchrist's disease.

Blastomycosis is defined as a chronic infection caused by the microorganism *Blastomyces dermatitidis.* This disease may resemble tuberculosis verrucosa cutis, syphilis, granuloma inguinale, drug eruptions, tricophytic granuloma, and gangrenous pyoderma.

The skin test, although available commercially, has not been in wide use and nothing more than presumptive value has been attributed to it.

Diagnostic Test. 0.1 ml. of the antigen is injected intradermally into the volar surface of the forearm. The reaction is interpreted at 12, 24, and 48 hours.

Source. Parke, Davis and Company, Detroit, Michigan.

Coccidioidomycosis

Synonym. Coccidioidal granuloma.

Coccidioidomycosis is a disease endemic in certain areas of California, as well as occurring sporadically in other parts of the world. The causative organism, *Coccidioides immitis,* has been isolated from the soil, vegetables, and from the internal organs of animals. This test serves as a diagnosis for the past or present infection of the fungus. Positive skin reactions develop early and the hypersensitivity may remain indefinitely. The coccidioidin test often becomes negative in the terminal stages of infection.

Diagnostic Test. 0.1 ml. of a 1:1,000 solution is injected, usually intradermally into the flexor surface of the forearm. If this test proves negative, 0.1 ml. of a 1:100 dilution is injected after 48 hours.

Source. Cutter Laboratories, Berkeley, California.

Histoplasmosis

Synonym. None listed.

Histoplasmosis is a disease caused by the fungus *Histoplasma capsulatum.* The organisms gain entrance into the body and produce a primary infection which may give rise to multiple calcium deposits in the lungs. The disease affects both children and adults (frequently infants), and in some ways resembles Kala-azar and American leishmaniasis. Primary infections are quite common in the central Mississippi Valley and the Ohio Valley. The disease is much more common than is suspected.

Diagnostic Test. There is good reason to believe that a positive cutaneous reaction to histoplasmin means past or present infection with *H. capsulatum.* Other fungus infections with related immunological properties can also cause reactions. The antigen may be of value in the differential diagnosis of pulmonary calcification, particularly in those areas where benign histoplasmosis is common. The test will not aid in the diagnosis of acute disseminated histoplasmosis since negative reactions are the rule, just as they are to tuberculin in the presence of miliary tuberculosis. In diagnosis it is necessary to do the histoplasmin, coccidioidin, and blastomycin tests simultaneously.

The concentrated histoplasmin is stable and if stored in a refrigerator should remain potent for several months. The stability of the dilution is not known but probably is maintained for at least two or three weeks. Peterson (*Pediatrics* 2:720, 1948), however, showed that dilutions of histoplasmin are probably stable for four or five months if kept refrigerated. Tests, after storage of the solution for one year in a refrigerator, showed no appreciable deterioration.

To prepare dilutions, the following apparatus is required: a flask containing sterile physiological salt solution (0.85 percent), a 10 ml. pipette with 0.1 ml. graduations, and wide-mouth, glass-stoppered bottles or suitable vials to hold the dilutions. Pipettes and bottles should be sterilized by boiling. Sterile technic and accurate measurements in making the dilutions are of prime importance. To 0.1 ml. of the histoplasmin concentrate add 9.9 ml. of diluent and mix thoroughly. This gives a 1:100 dilution and each 0.1 ml. contains 0.001 ml. of concentrate. This is too strong for routine skin testing. A 1:1,000 dilution is obtained by adding 1 ml. of the 1:100 dilution to 9 ml. of the salt solution. The skin test dose is contained in 0.1 ml. of the final dilution.

The test is carried out by injecting 0.1 ml. of the 1:1,000 histoplasmin intradermally into the forearm. A control test is not necessary. The syringe should not be used for performing tuberculin or other skin tests. The usual reaction consists of erythema with induration and a surrounding zone of edema measuring 0.5 cm. or more in diameter, which becomes maximum in 48 to 72 hours. Erythema alone is not considered an indication of sensitivity. Like tuberculin, histoplasmin

may give rise to a severe local reaction followed by necrosis and ulceration which may persist for several weeks.

Source. Parke, Davis and Company, Detroit, Michigan.

Sporotrichosis

Synonym. None listed:

Sporotrichosis is a chronic infection caused by the filamentous fungus *Sporotrichum schenckii.* This disease is characterized by the development in lymph nodes or subcutaneous tissues of nodular lesions, ulcers, or abscesses. Tuberculosis, blastomycosis, syphilis, and streptococcic infection may resemble sporotrichosis.

This test has little value since the causative agent is readily identified by its appearance in cultures. The organisms is generally obtained from unruptured nodules. The material is placed in Sabouraud's media and incubated at room temperature. The incubated material may then be examined under the microscope.

Diagnostic Test. 0.1 ml. of solution is injected intradermally into the volar surface of the forearm.

Source. Unknown.

Dermatophycosis and Dermatophytids

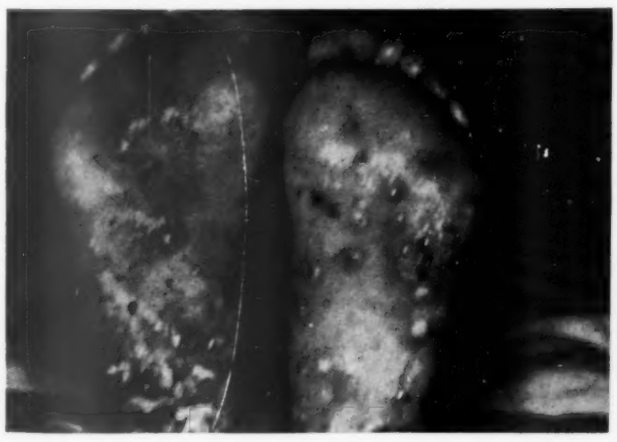
Synonym. None listed.

The dermatophytes belong to a closely related group of fungi, the species usually responsible for ringworm of the scalp, hands, beard, nails, and feet.

The dermatophytids are secondary cutaneous eruptions occurring in individuals who have become hyperreactive to the organisms or products of an existing dermatomycosis. The organism, *Trichophyton,* a subclassification of the dermatophytes, is used for the preparation of the fungus antigen Tricophyton.

Skin sensitivity to fungus antigens regularly accompanies the dermatophytids, and tests using these antigens are regarded as having considerable diagnostic value.

trichophyton mentagrophytes



Diagnostic Test. 0.1 ml. of a 1:30 dilution of Tricophyton is injected intradermally into the volar surface of the forearm. Stronger dilutions are apt to give a false positive reaction. A positive reaction signifies that the patient either has or has had an infection of more than minimal extent with a ringworm fungus.

Source. Hollister-Stier Laboratories, Los Angeles, California.

Moniliasis

Synonym. Candidiasis, oidiomycosis, thrush.

The yeast-like fungus, *Candida albicans,* is generally accepted as the etiological agent. Moniliasis causes a number of different types of lesions of the skin and mucous membranes. Candidiasis may occur as a superficial or systemic infection. The diagnosis is complicated by the fact that the causative organism may be isolated from many parts of the body of the normal individual. The diagnostic intradermal test, although available, is of little value and not recommended for general use. The direct microscopial examination is of more significance than other methods of diagnosis.

Diagnostic Test. 0.1 ml. is injected intradermally into the volar surface of the forearm.

Source. Hollister-Stier Laboratories, Los Angeles, California.

Protozoan Diseases

Toxoplasmosis

Synonyms. None listed.

Toxoplasmosis is an infection caused by the sporozoa *Toxoplasma gondii.* It is said to be frequently responsible for congenital chorioretinitis, mental deficiencies of infants, and some typhus-like infections.

The disease is both congenital and acquired. The acquired type possibly comes from sick pets, transmitted via sputum, saliva and feces. This form is likely to be asymptomatic, especially in adults, and invasion of almost every tissue may occur before detection.

Diagnostic Test. Intradermal injection is made of 0.1 ml. of the antigen and of a control. Positive reaction is apparent after 24 hours with erythema and induration of over 10 mm. A negative control reaction is evidence of past or persistent infection.

Source. The Eli Lilly Company, Indianapolis, Indiana, has material available for investigators' use.

Trichiniasis

Synonyms. Bachman test, trichinosis.

Trichiniasis is a disease caused by the infestation of the worm *Trichinella spiralis.* Infection in man is usually caused from eating insufficiently cooked pork. The intradermal test has proven of value in the diagnosis of this disease especially those cases exhibiting

vague symptoms. The infestation of the metazoan parasite has resulted in a high degree of dermal sensitization. Approximately 6 percent of the individuals showed a positive reaction, without clinical signs.

Diagnostic Test. 0.1 ml. of a 1:10,000 dilution is injected intradermally into the volar surface of the forearm. A control antigen using buffered saline is given at the same time.

There are two types of skin reactions, delayed and immediate. The delayed tuberculin-like reaction occurs early in the infection and has also been seen in long-standing quiescent cases. The immediate reaction occurs after the person has been infected two to three weeks. The delayed reaction reaches its maximum height in about 20 minutes and may subside so as to be called a doubtful reaction in about an hour. The immediate type reaction may disappear in 24 hours or may persist as a faint pink area.

Source. Lederle Laboratories, Pearl River, New York.

Echinococcus

Synonym. Casoni's test.

The cestodes and many of the trematodes are parasites dangerous to man. The hydatid cysts represent a larval stage of the tapeworm, *Echinococcus granulosus.* These cysts occur in the liver and other organs of man, cattle, horses, and sheep.

The antigen is fluid obtained by puncture of hydatid cysts of sheep, pigs, oxen, or human beings. The fluid is sterilized by filtration through selas 03 or fritted glass filter (F), and preserved in the refrigerator.

Diagnostic Test. The test is performed by injecting 0.01 ml. of a 1:100 or 1:10,000 solution of the antigen into the volar surface of the forearm. A positive reaction is indicated by an immediate local inflammation with erythema and edema rapidly appearing and spreading. The reaction reaches maximal intensity within 10 to 30 minutes, and begins to fade in one hour or less.

Positive reactions occur in 75 percent of the diseased patients but cross-reactions occur with other helminthic infestations, cancer of the liver, and jaundice.

Source. Hydatid cyst fluid is available from the National Institutes of Health, Bethesda, Maryland, in a 1:10,000 dilution. The Eli Lilly Company, Indianapolis, Indiana, also has material available for investigators' use.

Filariasis

Synonyms. Pachyderma, elephantiasis, hypersarcosis.

Elephantiasis is a disease of the tropics characterized by lymphedema, with resulting hypertrophy of the skin and subcutaneous tissue. The legs and scrotum are usually enlarged and deformed. Of the two species causing this disease, the most common is the filarial worm *Filaria (Wuchereria) bancrofti.*

The antigen is prepared from fresh canine *Dicrofilaria immitis.* A 1 percent suspension in normal saline is made from well-pulverized worm material. This material is incubated at 37° C. for one hour with frequent shaking, and left at room temperature overnight. The suspension is then centrifuged for 15 minutes at 4,000 r.p.m. and the supernatant fluid removed (1:100 dilution). A dilution to 1:10,000 is then made with normal saline. The antigen is sterilized by immersion in a water bath (56° C.) for one hour for three consecutive days. The material is then tested for sterility.

Diagnostic Test. 0.1 ml. of the material is injected intradermally into the volar surface of the forearm. Dog serum is used as a control.

An immediate wheal reaction may occur within 15 minutes, the criterion of positiveness being a difference in size between the test wheal and the control of at least 3 mm. A positive skin test indicates the presence of microfilarial. The antigen is effective but safe; but due to the necessity of fresh antigen, it is not very practical.

Source. The Eli Lilly Company, Indianapolis, Indiana, has material available for investigators' use.

Virus Diseases

Mumps

Synonym. Ender's test.

The skin test can be used as a means of revealing the majority of "normal" individuals who have in the past undergone apparent or inapparent infections and have therefore become immune. A negative reaction may signify in most instances susceptibility; but no prediction can be made as to whether the disease will develop or not. During a national emergency, mumps can be a crippling factor in the movement of troops. It is conceivable that, knowing immunity and susceptibility factors, proper immunization can be accomplished.

Enders, in 1943, prepared an antigen for skin testing using the heat-inactivated infected parotid gland of the monkey; the normal parotid gland was used as a control. The chick embryo antigen is now used commercially, although the problem of egg sensitive controls may be a complicating factor. The test is not infallible. Antibodies produced by the antigen may produce sufficient titer to invalidate serological tests which may be required later.

Diagnostic Test. 0.1 ml. of the antigen is injected into the flexor surface of the forearm. The reactions

are read in 18 to 36 to 48 hours. Those reactions producing a wheal under 10 mm. are considered negative.

Source. Lederle Laboratories, Pearl River, New York, and Eli Lilly Company, Indianapolis, Indiana.

Sarcoidosis

Synonyms. Nickerson-Kveim test, Boeck's sarcoid, pseudotuberculosis, Schaumann's disease, uveoparotid fever.

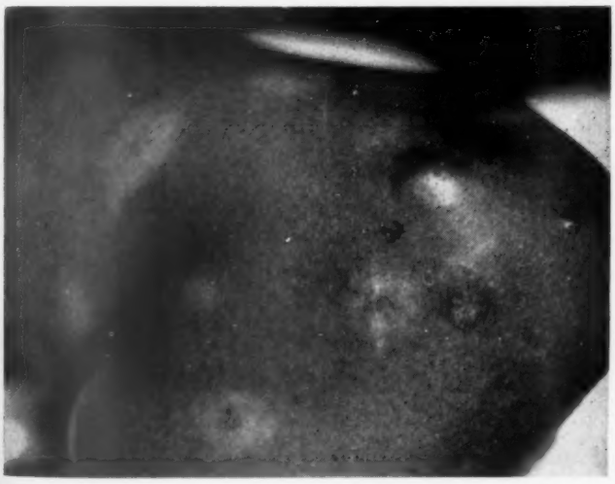
This disease, which probably is a peculiar form of tuberculosis, seldom produces serious symptoms, but persists for years. It begins in early life and progresses insidiously, producing lesions most often in the skin, lymph nodes, bones of the hands and feet, and lungs.

Diagnostic Test. A 10 percent suspension is made of proved sarcoid tissue in normal saline. The tissue is thoroughly ground and the larger particles are allowed to settle.

The suspension is heated to 60° C. for one hour on two consecutive days. Thimerosal 1:10,000 is added as a preservative. The material, after anerobic and aerobic tests for sterility, is stored at 40° C. In its final form the suspension is milky, containing in its sediment finely ground pulp, blood, stroma, etc. Seitz filtration is prohibited as the active material is not water-soluble but contained in the corpuscular elements of the sediment. The Kveim test may be expected to be positive in about 75 percent of active cases of sarcoidosis. The test usually becomes negative when the patient enters or is about to enter a stage of remission. The value of this test is somewhat limited.

0.15 ml. of the Kveim antigen is injected into the volar surface of the forearm. A papule occurs at the site of the injection and remains palpable for at least 60 days from the date of appearance. The site must be observed for from four to six months. The test site must be excised for histological examination.

sarcoidosis



Source. The material is available from Dr. Carl T. Nelson, Department of Dermatology, Columbia University, New York, New York; Dr. Richard D. Judge, University of Michigan, Ann Arbor, Michigan; and Dr. W. S. Middleton, Professor of Medicine, University of Wisconsin Medical School, Madison, Wisconsin.

Cat Scratch Disease

Synonyms. Non-bacterial regional-lymphadenitis, benign inoculum lymphoneticulosis.

Cat scratch disease usually begins with the development of an initial skin lesion a few days following a cat scratch. Other forms of inoculation are known, such as contact with other animals or a prick with a contaminated thorn.

Diagnostic Test. The pus obtained from the nodule capsule is the best source for material. Lymph nodes produce a very small quantity of inferior material. The method of preparation is similar to that of preparing free antigen. The pus is cultured aerobically and anaerobically, and especially for mycobacteria and fungi. The pus is diluted with sterile saline 1:4. The suspension is thoroughly mixed, and heated on a water bath at 60° C. for one hour on two consecutive days. Excessive heating inactivates the antigen. The final stage is to add, by rapid and thorough mixing with a sterile pipette, the last aliquot to make a 1:5 dilution of the original pus, using sterile 2.5 percent phenol in normal saline. No matter what volumes used, the fifth aliquot of phenol at 2.5 percent will bring all samples to a final concentration of 0.5 percent phenol. If all cultures remain sterile for 30 days, the antigen is safe to use. Tuberculin testing should be done.

0.1 ml. of the antigen is injected intradermally into the volar surface of the forearm. A raised indurated papule measuring 0.5 mm. to 1 cm. in diameter surrounded by an area of erythema will occur. The test is read in 48 hours. A positive reaction is a specific intradermal test in which there are no false positive reactions. Sensitivity to the antigen is persistent and may last from two to four years.

Source. Available for investigators' use from Dr. Lee Foshay, University of Cincinnati Medical School, Cincinnati, Ohio, and the South Bend Medical Foundation, Inc., 531 North Main, South Bend, Indiana.

Bacterial Diseases

Chancroid

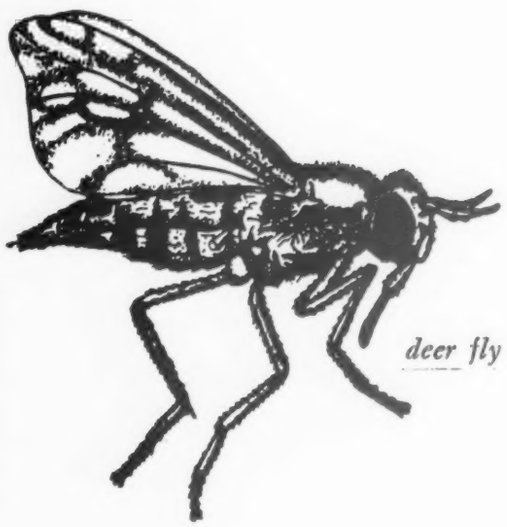
Synonyms. Ulcus molle, soft chancre, Ito-Reenstierna test, Ducrey test.

Chancroid is an infectious veneral disease caused by the bacillus *Hemophilus ducreyi*. The vaccine obtained from the bacillus *ducreyi* is occasionally used as an antigen for the diagnostic skin test. This test has limited value but is occasionally valuable in the diagnosis of chronic or atypical cases.

Diagnostic Test. Allergy is regularly established about two to five weeks after the onset of infection. The Ducrey antigen consists of the heat-killed suspension of the *H. ducreyi* organism, a gram-negative rod which usually appears in short-chained or parallel rows.

0.1 ml. is usually injected intradermally into the volar surface of the forearm. The reading is usually made at 48 and 72 hours. A negative reaction may be of particular value in excluding chancroid with chronic genital ulcers.

Source. Lederle Laboratories, Pearl River, New York.



Tularemia

Synonyms. Chara's disease, deer fly fever, rabbit fever.

Tularemia is a disease produced by the inoculation of the gram-negative organism *Pasteurella tularensis* in man by various wild animals and insects. It is a disease of increasing importance. It is now known to occur in practically all parts of the North American continent as well as in other parts of the world.

Diagnostic Test. The Foshay test is an intradermal skin test for the diagnosis of this disease. The test material consists of a detoxified antigen prepared by treating the suspended organism *P. tularensis* with nitrous acid. This test material is extremely valuable in the early diagnosis of the disease. It may become positive as early as three days after the onset of illness, whereby the serum agglutination reaction does not usually appear for about two weeks or later.

The usual dose is 0.1 ml. injected intradermally into the volar surface of the forearm.

Source. Lederle Laboratories, Pearl River, New York.

Summary

Sixteen diagnostic antigens are described. Where practical, the method of preparation and availability of these materials are described.

Although complement fixation tests are more accurate, skin tests are more desirable under certain conditions. This is especially true in military installations, both at home and overseas, where laboratory equipment may not be available.

Extensive interpretation of the results of these tests has not been attempted, since that is not within the realm of pharmacy.

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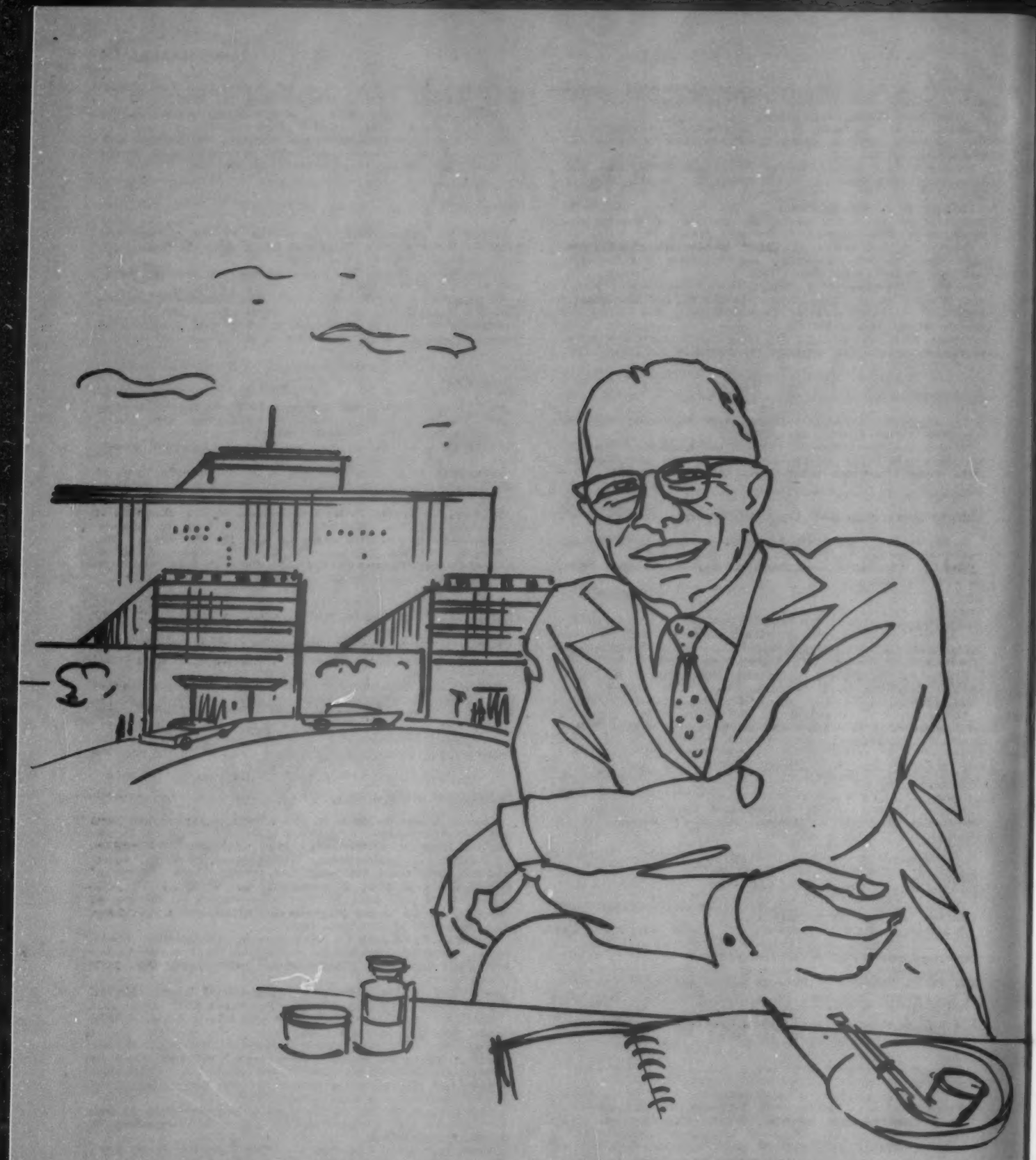

NEEDS

for Hospital Pharmacists in the United States

1957 through 1970

by GEORGE F. ARCHAMBAULT

► IN 1951, ACCORDING TO THE ANNUAL LISTING of the American Hospital Association, there were 6,832 hospitals in the United States. These hospitals had a bed capacity of 1,521,959. Of these hospitals, 3,117 reported that they operated pharmacies. Therefore 3,715 can be assumed as operating at that time without benefit of pharmacies.

In 1953, the American Hospital Association, for the first time, counted the pharmacists serving in the nation's hospitals. Pharmacists numbering 3,551 were reported as servicing the 3,245 pharmacies operating in hospitals. In 1953, the total number of hospitals was reported at 6,978 with a bed capacity of 1,580,654. The assumption can be made that 3,733 hospitals were operating without benefit of pharmacies, or stated another way there were 18 more hospitals without pharmacies than in 1951.

In 1955, the American Hospital Association's national survey listed 6,956 hospitals with a bed capacity of 1,604,408. These hospitals were serviced by 3,720 pharmacies staffed by 4,437 full-time and 915 part-time pharmacists. By difference, we can assume that in 1955 the nation had 3,236 hospitals *without* pharmacies. However, there were 497 more hospitals with pharmacies than the 1955 census report indicated.

Staffing

In 1956, the last year for which statistics are available, the American Hospital Association reported 6,966 hospitals with a bed capacity of 1,607,692. Of these hospitals, 3,773 were reported as being staffed by 4,713 full-time and 959 part-time pharmacists. It would appear, therefore, that currently in the United States, the hospital system operates 3,193 (45+%) hospitals *without* pharmacies, 43 less than in 1955, or 540 less than reported in the 1953 report.

In 1956, of the 6,966 hospitals listed, 5,299 were short-term general and special hospitals. Of this number, 857 were under 25 beds, 1,384 were 25 to 49 beds and 1,254 were 50 to 99 beds. These 3,495 hospitals of under 100 beds when compared to the 3,193 hospitals assumed as without pharmacy service give a reasonable hint as to where the majority of the deficiency in pharmacy service in hospitals now exists—in the small hospitals of 99 beds and less. This evidence is even more convincing when it is noted that Table 16 of the American Hospital Association's annual survey reveals that approximately 80 percent of the hospitals under 25 beds, 69 percent between 25 to 49 beds, and 48 percent between 50 to 99 beds do not support pharmacies.[2]

The AMERICAN SOCIETY OF HOSPITAL PHARMACISTS and other hospital and pharmacy associations are currently evaluating this problem in order to find practical solutions to the economic problems involved in providing competent pharmacy service in this neglected area.

YEAR*	HOSPITALS	BEDS	PHARMACISTS	PHARMACISTS FULL & PART-TIME	
1956	6,966	1,607,672	3,773	4,713	959
1955	6,956	1,604,408	3,720	4,437	915
1954	6,970	1,577,961	3,498	4,157	786
1953	6,978	1,580,654	3,245	3,551	not rep.
1952	6,903	1,561,809	3,245	not rep.	not rep.
1951	6,832	1,521,959	3,117	not rep.	not rep.

* Source. Administrator's Guide Issues, Journal of American Hospital Association, 1952 through 1957.

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Presented at the Fourth Pan-American Congress of Pharmacy and Biochemistry, Section on Hospital Pharmacy, November 1957, Washington, D. C.

There is presented in table form above the growth picture of hospitals in the United States, their pharmacies, and scope of utilization of pharmacists from 1951 through 1956.

Growth of Hospitals

To these statistics let me add the thinking of national hospital authorities relative to the future growth of the hospital structure of this country. Dr. John Cronin, Assistant Surgeon General, U. S. Public Health Services and Dr. Vane Hoge, currently Chief, Division of Hospital Facilities of the U. S. Public Health Service, and others, informed Congress in February (1957) that this nation is currently short some 840,000 beds and will add 30,000 hospital beds yearly in the immediate years that lie ahead, if the nation builds at the same rate as in the past 10 years. The present cost of bed construction is estimated at $16,000 per bed. Further, Congress was informed this growth will *not* keep pace with the nation's growing population, and backlog and annual obsolescence needs for beds. To meet such needs, 55,000 new beds are needed annually to keep pace with the population increase and obsolescence of present hospital plants. In fact, 30,000 beds are needed annually to keep pace with population growth alone.

The Bureau of Census estimates the population of this country at 209+ million in 1970. At current rates, the nation will have added some 390,000 beds to its hospital structure in the next 13 years. In 1970, the nation will have, if these estimates materialize, some two million beds in service.

One additional point requires discussion. A definite trend started to take shape in 1940 in connection with the construction of hospital beds and this trend is still with us. The number of hospitals appears to be increasing at a slower rate than in the past, but bed size within existing hospitals is on the increase. This is a significant development that hospital administrators and hospital pharmacists must evaluate in providing adequate, safe, legal pharmacy service to patients housed in hospital facilities.

Statistics of Pharmacists

To this picture of hospital pharmacy and general statistics let us now add some current statistics relative to community pharmacies and the pharmacist population of the nation. For these figures, the annual national census figures of the National Association of Boards of Pharmacy are used. It will be recalled that for 1955, the American Hospital Association reported 4,437 full-time and 915 part-time pharmacists on duty in the hospitals of the United States. For 1956, the figures given were 4,713 full-time and 959 part-time pharmacists.

Table 1. Pharmacists Employed in Hospitals, Continental United States, 1955*

Hospitals			Pharmacists		
Bed Size	No. of Hosp.	No. of Beds	Full-time	Part-time	Total
Hospitals Reporting 50 beds and over	2,597	1,233,000	4,271	785	5,056
Under 50 beds	240	7,400	166	130	296
Total	2,837	1,240,400	4,437	915	5,352
Hosp. Not Reporting 50 beds and over	2,101	185,000	No available data	No available data	No available data
Under 50 beds	2,018	179,000	No available data	No available data	No available data
Total	4,119	364,000	No available data	No available data	No available data
Total U. S. Hospitals	6,956	1,604,400			

*Source, American Hospital Association, *Hospitals*, Vol. 30, No. 15, Part 2, August 1, 1956.

The National Association of Boards of Pharmacy reported for these years as follows: 1956 (January 1, 1957) 52,351 community or retail pharmacies, a reduction of 328 from the 1955 figure. The number of pharmacists was reported at 110,688, a reduction of 304 from the 1955 report figure. The N.A.B.P. estimated that 3.6 percent of the pharmacist population of the nation was engaged in the specialty of hospital pharmacy as of December 31, 1956.*

Further, the N.A.B.P. reported that no more than 4,737 persons acquired a license for the first time in 1956. The N.A.B.P. also stated, because of its inability to determine exactly the number of individuals licensed in two or more states each year, that the exact number of pharmacists licensed in 1956 was much fewer than the 4,737 individuals reported by the several states as licensed.

The report of the Executive Committee of the American Association of Colleges of Pharmacy gives the 1956 enrollment in the schools of pharmacy at 16,927 undergraduates (3,773 seniors) and 655 graduate students. This number of seniors, 3,773, gives to a fairly accurate degree the number of potential licensees coming from the schools in the Spring of

*Women pharmacists approximate 38 percent of total in hospitals, and 6 percent in profession (38 percent of women pharmacists in hospitals are members of religious orders) according to the Hospital Pharmacy Survey done by Sass at the University of Chicago. See references.

1957. A similar breakdown presented in Chairman Zopf's (A.A.C.P.) chart shows 3,533 potential graduates for the spring of 1956. This figure appears to confirm the N.A.B.P.'s statement that much fewer than 4,737 individuals were licensed as practitioners of pharmacy in 1956 in the United States. While accurate statistics are not as yet available for the current year (1957), there is some indication that enrollment is below the 1956-57 level. The impact of the five-year program, effective in 1960, on the future supply of pharmacists is also an unknown factor.

With these vital statistics, let us project the actual utilization of pharmacists in the hospitals of the nation in the year 1956 through to 1970 in an effort to determine the number of pharmacists that will be required to service the hospitals and the impact of this demand on the schools of pharmacy and the general working population of pharmacists.

Hospitals with Pharmacists

Table 1. "Pharmacists Employed in Hospitals, Continental United States, 1955" illustrates the status of the nation's hospitals as of January 1, 1956. At that time, it will be noted, there were 6,956 hospitals in the United States and 2,837 of these reported pharmacists on their payrolls. Of these 2,837 hospitals, 2,597 were in the 50 beds and over class and 240 were in the under 50 beds grouping. This left 2,101 hospitals in the over 50 beds, and 2,018 hospitals in the under 50 bed listing, a total of 4,119 hospitals, without pharmacies. Concerning the bed capacity of the 6,956 facilities, it was reported that their beds numbered 1,604,000 and that the 2,837 hospitals with pharmacy coverage had 1,241,000 beds. This left 346,000 beds uncovered in the nation by pharmacy service.

Full-Time Hospital Pharmacists

Table 1 points out that the 2,837 hospitals of the nation having pharmacies employ 4,437 pharmacists full-time. Of this number, 4,271 are employed in hospitals of 50 beds and over and 166 are employed in the hospitals having under 50 beds. *The rate per 1,000 beds* calculated on these knowns (Table 2) is 2.76 pharmacists per 1,000 beds for the nation's hospitals, 3.58 for hospitals with pharmacies, 3.46 for hospitals with pharmacies in the 50 bed and over size and 22.2 for the hospitals with pharmacies in the under 50 bed size.

The rate per hospital of full-time pharmacists is also indicated in Table 2. For all hospitals the rate was 0.63; for hospitals with pharmacies, 1.56; for hospitals 50 beds and over with pharmacies, 1.64; and for hospitals under 50 beds with pharmacies, 0.69.

Part-Time Hospital Pharmacists

Table 1 reveals that in 1956, 915 part-time pharmacists were employed in the nation's hospitals. Of this number, 785 were in hospitals 50 beds and over and 130 in the hospitals under 50 beds in size.

The rate per 1,000 beds on part-time pharmacists (Table 2) was determined to be 0.57 for all hospitals; 0.73 for hospitals with pharmacies; 0.63 for 50 bed and over hospitals with pharmacies; and 17.5 for hospitals with pharmacies under 50 beds.

The rate per hospital for part-time pharmacists (Table 2) was 0.13 for all pharmacies; 0.32 for hospitals with pharmacies; 0.30 for hospitals 50 beds and over with pharmacies; and 0.54 for hospitals 50 beds and under with pharmacies.

Future Needs

Table 3 forecasts the estimated number of hospital beds in thousands in 1960, 1965 and 1970, as well as the need for full and part-time pharmacists in this period. Table 4 gives the more detailed presentation in this area.

In addition to the assumptions that the hospital bed growth of this country would be approximately 30,000 annually, that the present pharmacist ratio of 3.6 per 1,000 for new beds would be maintained (See Table 2—3.58 percent), and that the growth would be mainly within the number of hospitals currently in use, a replacement rate of 6 percent is assumed for the total period of projection.*

*The Hospital Pharmacy Survey done by Sass in 1955 at the University of Chicago reported this at 7 percent in his sampling, while the over-all pharmacy profession, through the N.A.B.P., reported 3.5 percent.

TABLE 2. RATIO OF PHARMACISTS PER 1000 BEDS AND PER HOSPITAL, 1955*

HOSPITALS	Ratio of Full-Time Pharmacists		Ratio of Part-Time Pharmacists	
Hospitals Reporting	Per 1000 beds	Per hospital	Per 1000 beds	Per hospital
50 beds and over	3.46	1.64	0.63	0.30
Under 50 beds	22.2	0.69	17.5	0.54
All Reporting hospitals	3.58	1.56	0.73	0.32
TOTAL U.S. HOSPITALS	2.76	0.63	0.57	0.13

*Based on the number of employed pharmacists reported by the 2,837 hospitals (From Table 1.)

TABLE 3. ESTIMATED NUMBER OF PHARMACISTS NEEDED IN 1960, 1965 AND 1970 FOR THE HOSPITALS WHICH REPORTED EMPLOYMENT OF PHARMACISTS.

YEAR	HOSPITAL PLANT		PHARMACISTS NEEDED	
ACTUAL	No. of Hospitals	No. of Beds	Full-Time	Part-Time
*1955	2,837	1,240,000	4,437	915
ESTIMATED				
1960	Unknown d	1,390,000(a)	5,000(b)	1,010(c)
1965	Unknown d	1,540,000(a)	5,500(b)	1,120(c)
1970	Unknown d	1,690,000(a)	6,050(b)	1,230(c)

*Source, American Hospital Association, *Hospitals*, August 1, 1956

(a) Based on an increase of 30,000 beds annually
(b) Based on present staffing rate of 3.58 pharmacists per 100 beds (from Table 2)
(c) Based on present staffing rate of 0.73 pharmacists per 1000 beds (from Table 2)
(d) Not predictable. Present trend indicates number of hospitals appears to be increasing at a slower rate than in the past with bed size in existing hospitals on the upswing. Number of hospitals with pharmacists can be assumed to increase in 1960, 1965 and 1970 over the 2,837 figure reported in 1955.

To cite a few forecasts of Table 4, it will be noted that for 1956, the number of hospital beds serviced by pharmacies was predicted at 1,270,000 and that a staff of 4,545 full-time hospital pharmacists would be needed to maintain the scope and degree of pharmacy service provided in 1955. How close did the projection forecast the future? Since the survey was made, the 1956 American Hospital Association figures have been reported.

The number of full-time hospital pharmacists predicted to be on duty was 4,545, an increase of 381 over the previous year. The number actually on duty was 4,713, an increase of 276 over the forecast. It is also interesting to note that the number of part-time pharmacists had increased to 959, from 915, in this one year period. From these figures one can only assume that the impact of the Minimum Standard for Pharmacy Service in Hospitals of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS and the recent decision of the Joint Commission on Accreditation of Hospitals to classify pharmacy service in hospitals as an *essential service* are already bearing fruit, and that the quality and scope of pharmacy service in hospitals are accelerating beyond the 1955 rate.

However, holding to the estimated requirements made in our conservative study (see Table 4) last April 1957, it will be noted that in 1958, pharmacy will be asked to produce 394 *new* hospital pharmacists. In 1964 we will need 433 and in 1970 we will require 472 pharmacists, a 15 year increase of 36 percent.

From the 1956 statistics of the American Hospital Association it would appear that from 500 to 600 full-time pharmacists will be closer to the actual annual replacement needs of hospitals. Concerning replacement, it will be noted that the study predicts that 108 pharmacists will be required annually for the expected 30,000 bed growth of the hospital structure of the nation in addition to 6 percent replacement factor of the annual hospital pharmacist working population.

Summary Analysis

This is a statistical report and projection of the needs for hospital pharmacies for the United States through 1970. The analysis and discussion include a review of the 1955 and 1956 statistics published by the American Hospital Association, the National Association of Boards of Pharmacy and the American Association of Colleges of Pharmacy as to pharmacy students, graduates, annual licensees, number of drug stores and number of pharmacists as well as the number of hospital pharmacists and hospital pharmacies.

A utilization factor of 2.76 full-time pharmacists per 1,000 beds for *all* hospitals, and of 3.6 full-time pharmacists per 1,000 beds for hospitals *with pharmacies* has been determined from the 1955 utilization of pharmacists as reported by the American Hospital Association (Table 1). A replacement factor of 6 percent is used in determining annual needs. For all hospitals the utilization rate was 0.63 full-time pharmacists per hospital or 1.56 full-time pharmacists for those hospitals employing full-time pharmacists.

An analysis of the 1955 American Hospital Association statistics on pharmacist utilization based on bed size of hospitals employing full-time pharmacists indicated a usage factor of:

(A) 3.46 full-time pharmacists per 1,000 beds in hospitals in the 50 bed and over grouping.
(B) 22.2 full-time pharmacists per 1,000 beds in hospitals in the 49 bed and less grouping.

Relative to hospitals, the factors were:

(A) 1.64 full-time pharmacists per hospital in the 50 bed and over grouping employing pharmacists, and
(B) 0.69 full-time pharmacists per hospital in the 49 bed and under grouping employing pharmacists.

The factor of 3.6 pharmacists per 1,000 beds in hospitals employing pharmacists allows for 108 new positions annually to service the 30,000 increased bed structure of the hospital system (Table 2). All factors are based on 1955 hospital staffing rates and statistics. No attempt was made to forecast additional pharmacist needs based on such factors as improved

quality of service or outpatient increase by reason of preventative medicine practices, third part payee, or geriatric prescription trends. The projection is intended to serve as a conservative estimate of hospital pharmacy manpower needs in the United States through 1970. The author points out that the projection is based only on the maintenance of the 1955 quality and scope of pharmacy care in the nation's hospitals and that no forecasting was attempted relative to an advance in quality or an expansion of pharmacy service in hospitals.

The first prediction plateau arrived at (4,545 full-time pharmacists on duty in 1956) is compared against the actual 1956 statistics. The 1956 survey reported 4,713 on duty, a gain of 276 full-time pharmacists in the one year period (4,437 in 1955) as against the estimated projection gain of 108 for the same period. In terms of all hospitals, the rate per full-time pharmacist per hospital has risen in the one year period from 0.63 to 0.67+.

This first test sampling of the validity of the projection schedule verifies that the estimated pharmacy manpower need is most conservative—a pleasant position for the rapid betterment of pharmacy service in the hospitals in the United States. Credit for this present spurt in the utilization of pharmacists in hospitals is given to the Joint Commission on Accreditation of Hospitals and the Minimum Standard for Pharmacy Service in Hospitals of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. The Joint Commission recently placed pharmacy service in the essential grouping. Pharmacy formerly was in the "desired" but not "essential" listing.

It appears that better than 10 percent of each year's pharmacist licensees (and presumably graduates) are now and will be entering this specialty of pharmacy* and that approximately 5 to 5.5 percent of the total working population of pharmacists in the United States are currently engaged in this type of pharmaceutical practice. These conclusions are based upon the following consideration: that less than 4,500 individuals are being licensed annually to practice pharmacy in the United States; that in 1956, 5,772 pharmacists (4,713 full-time and 959 part-time) were employed in hospital pharmacy; that an annual need is now proven for approximately 500 pharmacists (see Table 4 and 1956 statistics) in hospital work (new and replacement); and that the total pharmacist population of the nation is 110,668.

*It is interesting to note in connection with this 10 percent utilization factor, that the 1957 senior class of the Masssachusetts College of Pharmacy presented the following percentage breakdown of their career plans—retail practice, 75; teaching, 1; industry, 3; *hospital, 10*; research, 9; and other, 2.

TABLE 4. ESTIMATED REQUIREMENTS FOR FULL-TIME PHARMACISTS 1956-1970 IN THE HOSPITAL-WHICH REPORT EMPLOYMENT OF PHARMACISTS, SHOWING NET NEW NEED ANNUALLY.

YEAR	Projected No. of beds in the 2,837 hospitals based on 30,000 beds added ann.	Total No. of full-time pharmacists needed to maintain present staffing rate(a)	New Pharmacists Needed Annually		
			At 3.6 pharmacists 1000 beds for 30,000 new beds added annually	For replacement at 6% of Col. (3). (b)	Total Col. (4) plus Col. (5)
ACTUAL 1955	(2) 1,240,000	(3) 4,437	(4) xx	(5) xx	(6) xx
ESTIMAT'D 1956	1,270,000	4,545	108	273	381
1958	1,330,000	4,761	108	286	394
1960	1,390,000	4,977	108	299	407
1962	1,450,000	5,193	108	312	420
1964	1,510,000	5,409	108	325	433
1966	1,570,000	5,625	108	338	466
1968	1,630,000	5,841	108	351	459
1970	1,690,000	6,057	108	364	472
15 Yr. Increase	36%	36%	xx	xx	xx

(a). 3.58 pharmacists/1000 bed (from Table 2)

(b). Rate assumed from current data as follows: 3.5% for entire profession—N.A.B.P. Report, Oct.-Nov.-Dec., 1956. (110,992 Engaged in Practice—Census Date 1/1/56—1956 Proceedings Number, N.A.B.P.) 7+% for hospital pharmacists—Hospital Pharmacy Survey, Chicago Study, *The Bulletin of the American Society of Hospital Pharmacists 13* (Jan.-Feb.) 1956.

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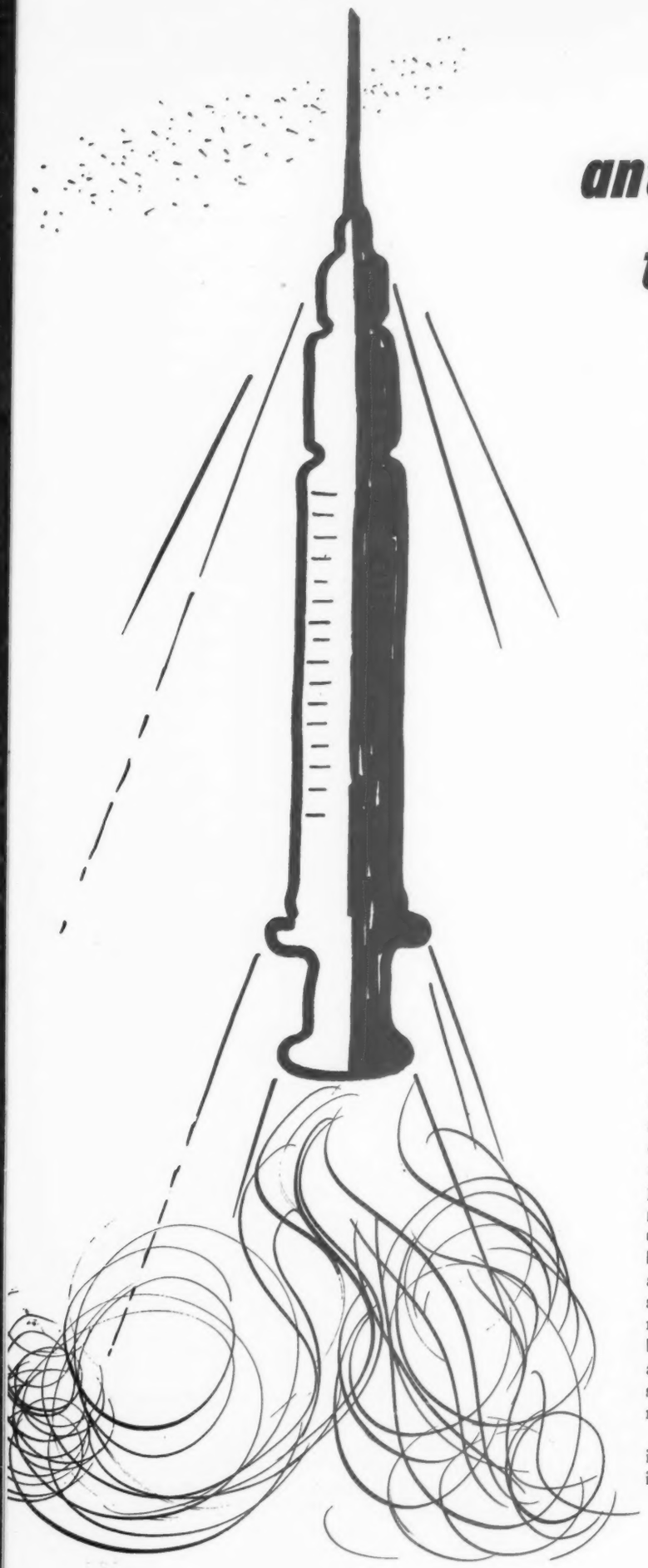

antibiotics today

(part II)

a summary of recent developments in antibiotics reported at the recent symposium on antibiotics held in Washington, D. C.

► THE FIFTH ANNUAL SYMPOSIUM on Antibiotics, sponsored by the Food and Drug Administration in collaboration with the journals *Antibiotics and Chemotherapy* and *Antibiotic Medicine and Clinical Therapy,* was held in Washington, D. C., October 2, 3, and 4. Recent discoveries and advances in the field of antibiotics were reported by leading scientists from the United States and abroad. A total of 161 papers were presented. This is part two of a summary which was begun in the January issue of the AMERICAN JOURNAL OF HOSPITAL PHARMACY.

OLEANDOMYCIN (Matromycin, Pfizer) is a basic antibiotic produced by a strain of *Streptomyces antibioticus.* Having the composition $C_{35}H_{61}NO_{12}$, oleandomycin is an entity composed of a unique nucleus termed oleandolite, to which sugar moieties desosamine and levo-oleandrose are glycosidically attached, according to Celmer and coworkers of Chas. Pfizer and Co.

Hobby and Lenert of Pfizer, reporting on observations on the mode of action of oleandomycin, presented evidence to show that oleandomycin may exert either a bactericidal or a bacteriostatic effect against susceptible microorganisms, depending to some extent upon the number of organisms present and/or the concentration of drug used and to a greater extent upon the time of observation. Oleandomycin, upon contact with susceptible microorganisms, promptly inhibits cell multiplication. Like the sulfonamides, it causes a decrease in the number of organisms only after five to seven hours in contact with organism. It is most active, moreover, as a bactericidal agent during that period following the period during which cell multiplication in the absence of the drug occurs most rapidly. The data presented suggest, but fail to establish conclusively, that cell mutiplication is essential to the action of this agent.

Elliott and Hall of the Veterans Administration Hospital in Minneapolis reported on the activity of oleandomycin, in combination with eight antibiotics, against staphylococci.

Oleandomycin, the penicillin salt of oleandomycin alone (Oleandopen) and with added penicillin G (compound APG) and oleandomycin with tetracycline (Signemycin) were tested individually and in combination with penicillin G, chloramphenicol, bacitracin, erythromycin, neomycin, tetracycline, novobiocin and vancomycin against 30 hospital strains of *Staphylococcus aureus*. Their activity was tested by tube dilution with subcultures and by paper strip-agar diffusion with replica plating.

Oleandomycin, its salts, and available mixtures were bacteriostatic and not bactericidal. Cross resistance between oleandomycin and erythromycin occurred with some strains. With strains resistant to penicillin and tetracycline, the oleandomycin salts and mixtures had the same activity as oleandomycin alone. There was no synergism observed with susceptible or resistant strains.

Oleandomycin preparations combined with 8 other antibiotics showed addition of bacteriostatic and bactericidal activities in about 50 percent of the cases. Synergism was not found. Antagonism of bactericidal activity was found in about 7 percent of the cases and was characteristic for some staphylococcal strains.

Sub-inhibitory concentrations of vancomycin stimulated growth of several strains of staphylococci in spite of high concentrations of oleandomycin.

Antibiotic mixtures were found to have an additive retarding effect upon the growth of staphylococci. Claims for synergism with oleandomycin mixtures could not be confirmed.

Oleandomycin and tetracycline were used in combination for the treatment of non-gonococcal urethritis by Willcox of St. Mary's Hospital, London, England. Sixty-two previously untreated cases of non-gonococcal urethritis were treated with Signemycin (6 Gm. over 6 days orally). Of 50 cases followed there have so far been only 6 failures (12 percent) within 3 months of post-treatment observation although not all patients have been observed for the full observation period. The tetracycline-oleandomycin combination was well-tolerated and has proved very useful indeed in the treatment of non-gonococcal urethritis.

Results of combined therapy in chronic urinary infections with sulfisoxazole and oleandomycin were reported by Lind and Trafton of the Lind Laboratories, Inc., Boston. In a series of over 40 cases the combination was found to be effective clinically against most gram-positive and certain gram-negative organisms associated with infections of the urinary tract, and to be especially helpful in chronic mixed infections. The combined drug was well-tolerated: more so than oleandomycin alone, but slightly less so than sulfisoxazole alone. In approximately 25 percent of the cases associated with gram-positive organisms, *in vitro* data showed them to be susceptible to the combination of sulfisoxazole and oleandomycin, yet resistant to penicillin and erythromycin. Although all of the gram-negative organisms were resistant to the combination, over 50 percent of the infections showed a favorable response clinically. The two drugs, although compatible, appear to act independently. There appears to be no evidence of potentiation or additive effect.

Some comments on the lack of synergism of tetracycline-oleandomycin mixture (Signemycin, Pfizer) were presented by Ross, Zaremba, and Puig of Children's Hospital, Washington, D.C. One hundred and sixty strains of *Staphylococcus aureus* were tested for minimal inhibitory concentrations against Signemycin and each of its component parts, tetracycline and oleandomycin. No synergism was demonstrable against any of these strains and, by and large, the effect of Signemycin proved to be a function of its tetracycline or oleandomycin content alone rather than a synergistic effect produced by the two components. Additional data obtained in a triple cross-over experiment with 15 members of the house staff at Children's Hospital similarly proved that the antistreptococcal and antistaphylococcal activity of the sera of the subjects showed no synergistic action when Signemycin was administered as compared to the antibacterial effect of the sera when either tetracycline or oleandomycin was administered separately.

An evaluation of parenteral oleandomycin in a pediatric hospital was presented by Asay and Koch of the Los Angeles Children's Hospital and the University of Southern California School of Medicine. This study was primarily concerned with the determination of serum and spinal fluid levels following intravenous and intramuscular administration of oleandomycin. Thirty hospitalized patients were selected for evaluation of serum levels, eight of which also had simultaneous cerebral spinal fluid level determinations. An additional 50 patients received the parenteral preparation and were observed for evidence of local reaction or general toxicity.

Serum levels after 100 mg./Kg./day given intramuscularly fell in the range of 10 ug./ml. after one hour and rapidly fell to 0.6 ug./ml. within 5 hours, whereas with 50 mg./Kg./day they were found to be in the range of 2.5 ug. after one hour and fell off to 0.3 ug. Levels were found to be slightly higher after intravenous administration. Cerebral spinal fluid levels after 100 mg./Kg./24 hours tended to be lower, in the range of 2.5 ug./ml. after one hour but remained in the range of 1.2 ug./ml. after 5 hours.

The drug was exceptionally well tolerated. There was no evidence of systemic toxicity or side reactions. Two patients developed slight redness and induration of the injection site after failure to rotate the sites of injections. There was no evidence of thrombophlebitis following continuous intravenous administration and no evidence of inflammation following extravasation of intravenous fluid into the subcutaneous tissues. In addition, one patient was treated by intraventricular administration of the drug after all other antibiotics had failed to eradicate a Staphylococcal aureus ventriculitis following a ventriculo-cardiac shunt for hydrocephalus. A prompt clinical and laboratory response was demonstrated with reduction of the cerebral spinal fluid cell count from 700 cells, 80 percent neutrophils to 2 cells both lymphocytes when she was discharged apparently well.

Results of a study of levels of oleandomycin and oleandomycin-tetracycline combinations in abnormal cerebrospinal fluid systems were reported by Melas, Lyons, and Covert of Albany Medical College. Twelve cases were studied in which there was either vascular, traumatic, or infectious disease of the central nervous system. These patients were given 30 mg. per kilogram of oleandomycin in a single intravenous dose. Serum and spinal fluid levels were studied by tube dilution method at varied intervals over a 24-hour period. Levels as high as 5 mcg. per ml. were found in the spinal fluid in the 4th and 6th hour. In two cases a supplementary dose of 500 mg. of tetracycline was given 6 hours after the dose of oleandomycin. Significant enhancement of bacteriocidal activity was noted on the test organism. In conclusion, the authors stated that oleandomycin produces adequate levels in the cerebrospinal fluid in abnormal systems. This level is enhanced by the addition of tetracycline.

The *in vitro* effects of oleandomycin-tetracycline on 202 cultures of *Micrococcus pyogenes* var. *aureus* were tested by

Oswald and Welch of the Food and Drug Administration, Washington, D.C. Two hundred and two coagulase-positive Micrococci, isolated from hospital patients in the Washington D.C. and Baltimore, Maryland areas were phage typed and tested for sensitivity to oleandomycin and tetracycline, alone and in combination. Using a serial dilution tube technic it was determined whether it took less, the same, or more of the agents in combination to accomplish complete inhibition than would be expected based on the fractional part of an MIC contributed by each member. It was found that these combined antibiotics acted synergistically against 65 of the 202 strains. Twenty-four of those organisms synergistically affected were phage-resistant and 41 were phage-susceptible. No antagonism was observed. The eleven cultures showing the greatest synergistic response were retested 9 times and the results were found to be reproducible.

Results of oleandomycin-tetracycline in human brucellosis therapy were reported by Molinelli, Barros, and Ithurralde of the Instituto Nacional de Microbiologia, Buenos Aires, Argentina. In six adult cases of occupational brucellosis (*Br. suis* 3 cases, *Br. abortus* 2, *Br. melitensis* 1) of common clinical form with febrile bacteremic picture, the combined treatment of tetracycline-oleandomycin in doses of 3 grams daily (750 mg. every 6 hours) during 14 days running (total dose 42 grams) produced in every case an immediate dramatic therapeutic effect, evinced by rapid normalization of temperature, euphoria, and quick general recovery. Fever disappeared at 48 and 51 hours in the 2 patients treated exclusively with tetracycline-oleandomycin and between 6 and 72 hours in 4 cases to whom, besides the above antibiotic mixture, 50 to 60 mg. prednisolone was given by mouth during the first 60 to 70 hours (5 mg. every 6 hours).

Treatment of chronic sinusitis with a combination of oleandomycin and tetracycline was reported by Tato and his coworkers. Twenty-eight patients with chronic sinusitis, who had failed or in whom the response to previous antibiotic therapy was inadequate, were given Signemycin orally in a dosage of one to two grams daily, in divided doses, for five and twelve days. In over one-half the patients therapy was completed by insertion of a permanent plastic catheter in the maxillary sinus, by means of which irrigation can be conducted. Results were considered excellent in 5, good in 13, poor in 7, unsatisfactory in one, and two patients were lost to observation.

Loughlin and Mullin of the New York Medical College one year ago, presented a preliminary report on the treatment of chronic intestinal amebiasis, yaws, lymphopathia venerea and tropical ulcer with a combination of oxytetracycline and oleandomycin (Matroterra, Pfizer) and Signemycin. At that time they noted that these antibiotic combinations were highly effective in the treatment of these infections. Since then, the authors have continued to enlarge the series of each of these diseases treated with Matroterra and Signemycin, and now report on the results of these studies in 429 cases, approximately one third having received the former and two thirds the latter. Thus, in 88 cases of chronic intestinal amebiasis, the diagnosis having been confirmed by standard laboratory techniques; 172 cases of yaws; 106 cases of lymphopathia venerea; and 65 cases of tropical ulcer were treated with dosages of these antibiotic combinations similar to those reported previously.

The same high degree of therapeutic effectiveness in each of these infections was maintained. Thus, only three cases of chronic intestinal amebiasis relapsed, one case of yaws was considered as a possible relapse; during periods of at least three months, there were no apparent relapses of lymphopathia venerea; and in tropical ulcer rapid healing was the rule in early cases, while in long-standing, exceptionally large and deep ulcers, although healing was slower, patients were rehabilitated within three to four weeks. The authors conclude that Matroterra and Signemycin have been the most effective antimicrobial agents that they have used in treating chronic intestinal amebiasis, yaws, lymphopathia venerea and tropical ulcer. In none of these cases was there any evidence of toxic or untoward reactions as a result of the administration of these antibiotic combinations.

PA-150, PA-153 and PA-166, new polyene antifungal antibiotics, were described by Koe, Tanner, Rao, Sobin, and Celmer of Chas. Pfizer and Co., Inc. Three different strains of *Streptomyces* have been encountered whose amphoteric antifungal elaboration products, termed PA-150, PA-153 and PA-166, have been characterized as new members of the extensive polyene group of antibiotics. A general three step procedure was found suitable for the isolation and purification of each antibiotic: 1) Alcohol extraction of the crude amphoteric antibiotic from mycelia; 2) Preparation of an appropriate crystalline salt; and 3) reconversion to the crystalline amphoteric form of the antibiotic. Low temperatures, an inert atmosphere and exclusion of light favored the stability of these polyene antibiotics, especially PA-150 which contains seven conjugated double bonds.

Reports of biologic properties of the new polyene antifungal antibiotics were given English and McBride of the Pfizer Therapeutic Institute, Maywood, New Jersey. PA-150 is highly active against strains of *Candida albicans* and *Saccharomyces cerevisiae*. Of 13 filamentous fungi pathogenic for man, ten were inhibited by 10 mcg./ml. or less. Of 22 phytopathogenic fungi, 16 were inhibited by 10 mcg./ml. or less. PA-150 inhibited 14 of 25 saprophytic fungi by 10 mcg./ml. or less. Marked toxicity in mice by the oral or subcutaneous routes was exhibited by PA-150.

PA-153 had very good activity against phytopathogenic and various saprophytic filamentous fungi. The minimum inhibitory concentration for all 47 species was 10 mcg./ml. or less. Of the 13 pathogenic fungi, 10 were inhibited by 10 mcg./ml. or less.

PA-166 had excellent activity against pathogenic, phytopathogenic, and saprophytic fungi. An average minimum inhibitory concentration against *Candida albicans* was 0.78 mcg./ml. PA-166 failed to protect mice against experimental *Candida albicans* infection after oral, subcutaneous, or intravenous administration. The acute oral toxicity (LD_{50}) of PA-166 is greater than 200 mg./Kg. The acute subcutaneous toxicity is greater than 800 mg./Kg.; and the acute intravenous toxicity (LD_{50}) is between 12.5 and 25 mg./Kg. in mice.

PENICILLIN V was the subject of three papers at the Antibiotics Conference. Peck and Griffith of the Lilly Laboratory for Clinical Research, Indianapolis General Hospital, reported comparative clinical laboratory studies of potassium penicillin V and acid penicillin V. Their studies confirmed that soluble salts of penicillin V give higher initial blood levels more rapidly than acid penicillin V. Ten fasting subjects received both acid and potassium penicillin V. Serum penicillin assays at 15, 30 and 60 minutes after the administration of the potassium salt were 50 to 100 percent higher than equivalent doses of acid penicillin V. There was no difference between these preparations when assays were made at 2, 4 and 6 hours.

After a standard meal, serum penicillin assays were almost identical following the potassium salt of penicillin V as after

ingestion of the acid form. The onset of the high levels was slower, the peaks not as high, but the assays remained higher for a longer period. There was just as much penicillin absorbed when penicillin V was given with meals as when the acid form of penicillin V was given fasting. Because of the higher initial levels during the fasting state and equal levels to penicillin V when given with food, potassium penicillin V is believed to be superior to the acid form of penicillin V.

The relative clinical effectiveness of oral penicillin G as compared to penicillin V was reported by Lombardi, Boyd, and Nightingale of the Flower and Fifth Avenue Hospitals, New York City. This investigation was undertaken to study the effectiveness of oral penicillin G as compared with oral penicillin V in the treatment of the common infections encountered in the general practice of medicine. The authors were primarily interested in their usefulness in mild to moderate infections, and prophylactically in susceptible patients in whom it is important to lessen the incidence of infections. It is the authors opinion that the severe infections that occur in hospital practice are best treated by the parenteral administration of penicillin. One-hundred and thirty-six subjects were selected with various acute infections which upon culture revealed the presence of organisms sensitive to penicillin. The selection of patients was largely predicated upon the possibility of using oral penicillin G in one and equal amounts of oral penicillin V in another with a similar syndrome; however, it was limited to those in whom adjuvant therapy could be kept at a minimum. The blood levels of penicillin were not determined in this series, the criteria of effectiveness being based on the clinical appraisal of the course of the illness. Results indicate that oral penicillin G is as effective and as desirable as oral penicillin V in the treatment of these infections. The authors were very impressed with the satisfactory therapeutic responses that are easily and safely obtained with oral penicillin G and oral penicillin V. They conclude that these antibiotics can be used satisfactorily and can replace parenteral penicillin in the great majority of infectious diseases seen in office practice and in the outpatient department.

Prevention of streptococcal infections in rheumatic fever subjects using penicillin G, penicillin V, and benzathine penicillin was reported by Massell, Miller, Stancer, Vecchiolla, and Young of the House of the Good Samaritan in Boston. Reduction of group A streptococcal infection by prophylaxis was measured by comparing infection rates in ambulatory rheumatic children, given penicillin, with rates in their siblings, not given penicillin. The common environment made the siblings ideal controls. Studies included throat cultures, antistreptolysin-O tests, and home visits at time of illness. Total person-weeks of observation to date are 12,762 for the rheumatic children and 16,551 for their siblings.

Results indicate that prophylaxis was effective for prevention of streptococcal infection, though degree of effectiveness varied somewhat with the penicillin regimen and with definition of group A streptococcal infection. Intramuscular benzathine penicillin gave the most consistently high reduction of infection rate. Oral buffered penicillin G and oral penicillin V did not differ appreciably in effect; both caused high reduction of symptomatic infection but lower reductions of asymptomatic streptococcal infection and infection with an increase of antistreptolysin-O. Two definite and one possible rheumatic fever recurrence occurred in patients on oral penicillin G; none in those on oral penicillin V and none in those on intramuscular benzathine penicillin.

PENICILLINASE, an enzyme that hydrolyzes and inactivates penicillin, has not previously been given to human patients for therapeutic evaluation. Murray C. Zimmerman of the Department of Medicine, University of Southern California reported the results of treatment by injection of penicillinase in 50 patients with allergic reactions due to penicillin. Many of these patients had reactions of weeks or months duration, unresponsive to previous treatment with antihistamines, calcium, steroids, ACTH, and other conventional therapy. Penicillinase gave rapid symptomatic relief. There was no recurrence of symptoms when treatment was stopped in most of these patients.

The *in vivo* penicillin-inactivating effect and toxicity of penicillinase was described by Chen, Bard, and Balsito of the Department of Pharmacology, Marquette University School of Medicine, Milwaukee. Using a modified Kolmer's method, the activity of a highly purified penicillinase preparation was studied in rabbits given penicillin, both penicillin and penicillinase being injected intramuscularly. The minimum dose of penicillinase required to inactivate 100,000 and 50,000 units of either crystalline or procaine penicillin G was found to be in the order of 5,000 and 2,000 units respectively. A single injection of 5,000 units of penicillinase completely inactivated 100,000 units of crystalline penicillin given simultaneously with and repeated 8 hours after penicillinase. Considerable penicillin-inactivating activity remained as long as 4 days, as evidenced by a marked reduction of penicillin blood levels following repeated injections of penicillin.

Acute and short-term chronic toxicity studies indicate that penicillinase is practically nontoxic. Doses up to 10 million units/Kg. were well tolerated intramuscularly in rabbits, rats, and mice. No adverse effects were observed in dogs, rats and mice receiving 200,000 units/Kg./day for a period of 6 weeks. No hypersensitivity or anaphylactic reactions were shown in guinea pigs following the second and third injection of penicillinase given at intervals of 8 to 10 days.

PHENYL PARA-AMINOSALICYLIC ACID, Tebanyl, a new tuberculostatic agent, was discussed by Meyer. Its use is the same as PAS, i.e., to prevent the development of resistance of strains of tubercule bacillus to streptomycin and isoniazid. The great advantage appears to be the small percentage of intolerances, gastrointestinal symptoms, and stronger anti-resistant effect as compared with PAS.

Phenyl PAS is 80 percent absorbed because it is micronized and treated with surface active agents. It is indicated in all cases where PAS cannot be taken, and therefore continuous treatment is possible. There are no contraindications to its use except drug fever and rash. Phenyl PAS has a pleasant taste and in many cases the patient's appetite has improved

Phenyl PAS is given in doses of 4 Gm. three times daily with meals, suspended in water or milk. Clinical studies in Denmark have indicated good results with phenyl PAS. This report is the first American trial of phenyl PAS.

PIMARICIN is a new crystalline antifungal antibiotic of polyene structure isolated from the culture filtrate of *Streptomyces natalensis nov. spec.* Its structural formula is: $C_{30-32}H_{45-50}NO_{13}$. This antibiotic is active against a wide variety of pathogenic and non-pathogenic fungi and yeast species in concentrations of 1 to 10 ug./ml. There is no, or negligible, activity against bacteria. Results of studies on pimaricin were presented by Struyk, Hoette, Drost, Waisvisz, van Eek, and Doogerheide of the Royal Dutch Yeast and Fermentation Industries, Delft, Holland. Daily oral administration of 50 to 100 mg./Kg. body weight to rats for a period of ten weeks was tolerated well. Addition of pimaricin (50 p.p.m.) to the feed of rats either with or without 200 p.p.m. tetracycline

reduced the yeast count of the feces to practically zero. Clinical evaluation of pimaricin is in progress.

RISTOCETINS A and B are two new antibiotics isolated from the fermentation beer of *Nocardia lurida*. They are essentially similar in their physico-chemical and antimicrobial properties except that ristocetin B is 3 to 4 times more potent than ristocetin A. A study by Hwang, Primack, Stein, and Richards of Abbott Laboratories revealed that both antibiotics or mixture of both of various purity, had relatively low toxicity. Ristocetin B was about 3 times as toxic (intravenous, mouse) and irritating (intramuscular, rabbit) as ristocetin A on a weight basis. There were no essential differences in their pharmacodynamic properties and fate after intravenous administration. Both antibiotics were apparently excreted exclusively by the kidneys and did not appear in the cerebrospinal fluid, aqueous humor, or saliva. Simultaneous renal clearances of ristocetin A and creatinine were measured in the dog. Apparently glomerular filtration and tubular reabsorption were involved in the renal excretion of ristocetin A. After prolonged daily intravenous administration to rabbits and dogs at relatively high doses no abnormal laboratory or histological findings attributed to the antibiotic preparation were obtained.

Grundy and coworkers at Abbott Laboratories made a comparative study of crystalline preparations of ristocetins A and B *in vitro* and *in vivo*. Their antimicrobial spectra employing 44 microorganisms were determined and the development of resistance was studied using two strains of *Staphylococcus aureus*, one of *Staphylococcus albus* and two enterococci. Ristocetin B proved to be three to four times more active than ristocetin A both *in vitro* and *in vivo*. No differences in antimicrobial spectra were detected. Resistance to either antibiotic or the combination was not readily developed. A greater degree of resistance to ristocetin A than to ristocetin B was observed in three resistant cultures. These differences were not great, but appear to be significant. The two antibiotics were additive in effect in mouse protection tests.

Holper, Rickher, and Sylvester of Abbott Laboratories studied the *in vivo* activity of gamma globulin when used in combination with ristocetin in experimental bacterial infections in mice. Ristocetin alone and in combination with gamma globulin was studied in mice infected with *Staphylococcus aureus*, Smith, *Streptococcus pyogenes*, C-203 M, and *Diplococcus pneumoniae*, Type I. The activity of gamma globulin alone was determined with each bacterial infection studied. Results indicated as much as 50 percent greater protection in infected mice treated with gamma globulin plus ristocetin, as compared to animals treated with ristocetin or gamma globulin alone. Although the combination of gamma globulin with ristocetin gave increased protection at all levels of antibiotic, the enhanced effect was particularly pronounced at low levels of ristocetin. Gamma globulin potentiated the activity of ristocetin with all the experimental infections studied.

The use of ristocetin (Spontin, Abbott) in the treatment of antibiotic-resistant staphylococcal pneumonia was reported by Calvy of the U. S. Naval Hospital, St. Albans, New York. Clinical studies demonstrated the usefulness of the ristocetin in the treatment of antibiotic resistant staphylococcal pneumonia. In a six-month period during the course of a serious outbreak of hospital acquired staphylococcal infections (hemolytic staphylococcus aureus, coagulase positive) a total of seven cases of staphylococcal pneumonia were encountered. The index case followed a fulminant fatal course of 96 hours despite administration of penicillin, streptomycin, and novobiocin. The recovered organism was resistant to the foregoing antibiotics. One child and one young adult responded to chloramphenicol, penicillin, and streptomycin in spite of *in vitro* studies which indicated resistance. Following this experience, four successive critically ill, near-moribund patients with the same disease were given large doses of penicillin along with streptomycin, erythromycin, etc. without satisfactory response. Sensitivity tests revealed resistance to all of the foregoing agents. Two of these cases had spontaneous pneumothorax and one developed a lung abscess.

Ristocetin became available at this time and was promptly put to use. Clinical improvement in each case with temperature fall by lysis, beginning resolution of pneumonia, and general improvement in sense of wellbeing followed directly, within 24 to 48 hours. The patient with the lung abscess responded promptly with general improvement and fall of temperature from 104°F. to 99°F. in 12 hours. Ristocetin was given intravenously every 4 hours in dosage up to 500 mg. with gradual tapering during courses of therapy that were continued as long as one month. Continuous intravenous alimentation was required and the medication was injected into the tubing. No untoward reactions, save for mild tachyphylaxis, were observed.

Successful short-term therapy of enterococcal and staphylococcal endocarditis was reported by Romansky, Holmes, and Holmes of the George Washington University School of Medicine and the District of Columbia General Hospital, Washington, D. C. In five of the six patients with enterococcal endocarditis the microorganism was found to be resistant to penicillin and streptomycin, and sensitive to 0.1 to 0.3 units per milliliter of ristocetin. In the patient with endocarditis due to the hemolytic *Staphylococcus aureus* the microorganism was sensitive to penicillin, streptomycin, erythromycin, chloramphenicol, tetracycline, novobiocin, and to 1.0 unit per milliliter of ristocetin. In these seven patients the period of ristocetin therapy ranged from 10 to 24 days (average duration 16 days). Approximately 2 grams per day given intravenously in two doses, for approximately 2 weeks, appears to be adequate therapy. A satisfactory clinical and bacteriologic response was observed in these patients, the longest follow-up being 18 months. Two of the seven patients developed a transient neutropenia while on ristocetin therapy.

SULFOCIDIN is a new antibiotic isolated from the broth of a previously undescribed strain of Streptomyces and has been reported by Zief, Woodside, and Ham of J. T. Baker Chemical Co. Sulfocidin is active against gram-positive and gram-negative bacteria, mycobacteria, and fungi. It is strongly bactericidal to gram-positive bacteria. The low concentration required against most gram-positive bacteria (0.01-0.3 ug./ml.) was particularly striking. Bioautographs with 3 percent aqueous ammonium chloride gave four sterile zones using *S. lutea* (R_f 0.0, 0.06, 0.13 and 0.30).

Sulfocidin is a neutral substance soluble in chloroform, acetone, lower alcohols, 1,4-dioxane, pyridine, and ethyl acetate. It is insoluble in water, 10 percent hydrochloric acid, 10 percent sodium bicarbonate solution, carbon tetrachloride, and petroleum ether. The ultraviolet absorption spectrum of an ethanolic solution exhibited end absorption with a shoulder at 282 mu.

The following tests were negative: ninhydrin, Sakaguchi, maltol, ferric chloride, Fehling's, biuret, nitrochromic acid, 2,4-dinitrophenylhydrazine, and anhydrous aluminum chloride. Sulfocidin decolorizes a solution of potassium permanganate in acetone in the cold.

Acute toxicity studies carried out in mature, male, 20 Gm. albino mice show an LD_{50} (I.P.) of 1-5 mg./Kg.

The effect of sulfocidin on transplantable tumors in mice was described by Pugh, Lechevalier, Braun, and Waksman of the Institute of Microbiology at Rutgers University. These investigators found that preparations of this antibiotic have therapeutic effects against the ascitic form of Gardner's lymphosarcoma (6C3HED) and sarcoma 180 in mice. Used alone they have no effect against the solid form of sarcoma 180 and adenocarcinoma C3HBA in mice.

In experiments with the lymphosarcoma, the average survival time was increased by 33 days when the mice received intraperitoneally 5 mcg. each, 24 hours after implantation of the tumor. The average survival time was increased by more than 56 days when the mice received subcutaneously 2.5 mcg. each daily for five days. The percentage of tumor cells in the ascitic fluid of treated animals decreased rapidly and remained at a low level ($<$ 5 percent of ascites cells) for periods up to 3 weeks.

In experiments with the ascitic form of sarcoma 180, treatment was still effective if delayed until 48 hours after implantation of the carcoma cells. No synergistic effect against ascitic lymphosarcoma or solid sarcoma 180 was noted when suboptimal amounts of actinomycin D were administered in combination with sulfocidin.

Early results indicate that a crystalline preparation of sulfocidin also has some antitumor activity.

TELOMYCIN is a new antibiotic isolated from an unidentified species of Actinomycete by Misiek, Fardig, Gourevitch, Johnson, Hooper, and Lein of the Research Division of Bristol Laboratories, Inc. The antibiotic, a polypeptide, is active against gram-positive bacteria. Telomycin has been isolated by solvent extraction procedures and differentiated by chemical and physical properties from other polypeptide antibiotics.

Telomycin is active *in vivo* protecting mice infected with *Micrococcus pyogenes* var. *aureus* and *Diplococcus pneumoniae*. Treatment intramuscularly at the time of infection gave a CD_{50} of 20 mg./Kg. for *Diplococcus pneumoniae*. The acute toxicity by the intraperitoneal route was found to be greater than 500 mg./Kg.

Microbiological studies on Telomycin were described by Gourevitch, Hunt, Moses, Zangari, Puglisi, and Lein of the Research Division of Bristol Laboratories, Inc. Telomycin is active against strains of *Micrococcus pyogenes* var. *aureus*. *In vitro* data indicate that *Micrococcus pyogenes* develops resistance to Telomycin at a slow rate. Its activity depends on the inoculum size and the medium. In 100 percent serum it shows its greatest activity. *In vivo*, Telomycin is effective against acute and chronic *Micrococcus pyogenes* infections in mice. It is at least as effective as penicillin in clearing kidneys of *Micrococcus pyogenes* in long term infection.

Pharmacologic studies with Telomycin were reported by Tisch, Huftalen, and Dickison of the Research Division of Bristol Laboratories, Inc. Telomycin has been found to have an LD_{50} in mice of $>$1000 mg./Kg. when given by the oral, intravenous, intramuscular, or intraperitoneal route. Irritation studies have been carried out in rats, rabbits, and dogs following intramuscular administration. Blood level studies in rabbits and dogs have shown that serum concentrations of 1 to 2 units are obtained during the first six hours for each mg. of Telomycin given by the intramuscular route. Blood levels following the intramuscular injection of 20 mg./Kg. persist through sixteen hours. No oral blood levels have been obtained at the doses employed. Six weeks of subchronic toxicity studies in dogs have shown that intramuscular injections of 200 mg./day are well tolerated. The antibiotic seems worthy of clinical trial.

TETRACYCLINE phosphate and tetracycline with sodium metaphosphate were the subjects of numerous papers at the Antibiotic Conference. Several of these papers were reports on the blood levels achieved with these derivatives of tetracycline compared to those achieved with the hydrochloride salt. Tall, Gaskill, and Coriell of the South Jersey Medical Research Foundation and Municipal Hospital, Camden, N. J., reported on blood levels attained in pediatric patients and in adults. Crossover studies involving 12 adult subjects who received single doses of 250 mg. of tetracycline phosphate and tetracycline hydrochloride 48 hours apart resulted in higher average blood levels for tetracycline phosphate than for tetracycline hydrochloride. However, when single large doses (1,000 to 2,000 mg.) were given to 5 adult subjects 91 hours apart, higher blood levels were obtained with tetracycline hydrochloride. This could not be explained. Results of serum assays on 9 pediatric patients show consistently adequate levels after ingestion of various doses of tetracycline phosphate. In 7 pediatric patients with scarlet fever treated with tetracycline phosphate the laboratory and clinical response was equal to oral penicillin and superior to novobiocin.

Absorption, diffusion, and excretion studies on the phosphate complex salt of tetracycline by Shidlovsky, Prigot, de L. Maynard, Felix, and Hjelt-Harvey of Harlem Hospital, New York, N. Y., employed hospitalized patients in crossover experiments with tetracycline phosphate complex (Tetrex, Bristol) and tetracycline hydrochloride. Assays confirmed that the activity following the administration of the tetracycline phosphate complex surpasses that of the hydrochloride salt. With the intramuscular route, higher levels are achieved more rapidly than by the oral. Antibiotic activity is demonstrable in the blood, urine, bile, amniotic fluid, placental cord serum, and human milk. In non-inflammatory spinal fluids from patients under this study, no activity was detected.

Hueber, Doujak, and Spitzy of the University Hospital in Vienna, Austria, reported results of clinical studies with Achromycin V (base of Achromycin with sodium metaphosphate). In a series of patients with febrile diseases the therapeutic effect and the serum levels of orally dispensed Achromycin V (base of Achromycin with added sodium metaphosphate) were studied. After a single oral dose of Achromycin V surprisingly higher serum levels were found above those which were obtained with Achromycin hydrochloride. The average values in 7 patients were: 0.29 after one hour; 1.21 after 3 hours; 0.9 after 6 hours; 0.41 after 9 hours and 0.11 ug./ml. after 24 hours. When 250 mg. of Achromycin V were given continuously every 6 hours serum levels of 4 to 10 ug./ml. were obtained. However, if 250 mg. Achromycin V were only given every 12 hours the serum levels were between 1.5 and 3.4 ug./ml.

Trafton and Lind of the Lind Laboratories, Inc., Boston, reported that the effectiveness of tetracycline phosphate complex, clinically and bacteriologically, in urinary infections, appeared to be comparable to that of tetracycline hydrochloride, but not superior.

INTRAMUSCULAR tetracycline phosphate was the subject of several papers. A new concentrated tetracycline phosphate complex aqueous solution for intramuscular injection was described by Buckwalter, Albright, and Kaplan of Bristol Laboratories. This solution contains Xylocaine hydrochloride, ascorbic acid, a magnesium salt, and tetracycline phosphate complex. Concentrations of 250 mg. of

tetracycline hydrochloride activity as tetracycline phosphate complex per ml. have been obtained. Solutions of this concentration are not possible under the same conditions with tetracycline hydrochloride. Tetracycline serum concentrations in human subjects indicated that these products are well absorbed and show repository action.

Serum concentration and local tolerance in infants and young children of intramuscular tetracycline phosphate complex were reported on by Portney, Draper, and Wehrle of the State University of New York, Upstate Medical Center, Syracuse, N.Y. Sustained levels of approximately 1 ug. were observed in young children as long as 24 hours following intramuscular injection of a single dose of 25 mg./Kg. of tetracycline phosphate complex.

Cohn and Longacre of the Louisiana State University, New Orleans, found that a single daily intramuscular injection of 250 mg. of tetracycline phosphate produced satisfactory serum levels.

Local pain response and blood levels in geriatric patients were evaluated by Dube of the Van Duyn Memorial County Hospital, Onodaga, N.Y. In an attempt to evaluate the local pain response and blood levels in older patients, tetracycline phosphate complex was administered intramuscularly to groups of twelve patients in doses of 100 mg., 250 mg., and 500 mg., of tetracycline hydrochloride activity. Reference standards of tetracycline hydrochloride suspensions and saline solutions were injected into the same patients. All patients received a simultaneous injection of saline and the results of each test preparation were compared with the pain response to saline. In addition, multiple 12-hour injections over an 8 day period were given to nine patients using 250 and 500 mg. of tetracycline phosphate complex.

As a separate experiment, blood levels following single injections of 250 mg., and 500 mg., tetracycline phosphate complex were obtained at 1, 3, 24, and 48 hours in groups of ten patients each. In addition, blood levels were obtained following injections every 12 hours of the 250 and 500 mg., tetracycline phosphate complex over a 7 day period in nine patients.

The results obtained are as follows: (1) Single intramuscular injections of 100 mg., 250 mg., and 500 mg., tetracycline phosphate complex were not significantly more painful than saline or the tetracycline reference standard injections when compared with saline controls. (2) Multiple doses of 250 mg., tetracycline phosphate appear to be well tolerated, but multiple 500 mg., injections were too painful for prolonged use. (3) Blood levels following 250 mg., single injections of tetracycline phosphate complex averaged 1.8 micrograms per ml. at 1 hour, 1.2 micrograms per ml. at 3 hours and 0.6 micrograms per ml. at 24 hours, and 0.3 micrograms per ml. at 48 hours. Blood levels following 500 mg., single injections of tetracycline phosphate complex averaged 2.3 micrograms per ml. at 1 hour, 2.2 micrograms per ml. at 3 hours, 1.1 micrograms per ml. at 24 hours, and 0.6 micrograms per ml. at 48 hours. (4) Blood levels obtained after multiple injections of 500 mg., of tetracycline phosphate complex averaged 4.56 micrograms per ml. after 3 days. Blood levels obtained after multiple injections of 250 mg. of tetracycline phosphate complex averaged 3.87 micrograms per ml. after 3 days.

Correction of simple growth failure in tropical children with low level doses of Terramycin or lysine was discussed by Loughlin, Joseph, and Alcindor of the New York Medical College, New York. In tropical children, the relation of simple growth failure to undernutrition has been recognized for many years. However, correcting the undernutrition by supplying diets rich in high quality proteins, including milk, has not been economically practicable because foodstuffs either are unavailable or are too expensive. The demonstration that antibiotics, including Terramycin, and other substances, such as lysine, have growth stimulating effects on children in temperate zones pointed the way to this study—in which the diets of tropical children were to be kept unchanged and therefore deficient in protein and calories, but to which oxytetracylcine in low level doses or lysine would be added daily as supplements.

Sixty-four children at a rural school in Haiti were selected as suffering from "stabilized growth failure" after six months of control measurements charted on Wetzel grids had been analyzed. From that point on, the investigation was conducted as a "triple blind study." The children were separated into four matched or equalized groups. After the groups had been arranged thus, three supplements—10 mg. and 50 mg. of oxytetracycline, and 1 Gm. of lysine were assigned by random selection, one to each of three groups, while a fourth, receiving placebos, served as a control. The supplements and placebos were coded, and were known only to the persons who had assigned them to the groups, but not to those concerned with measuring the children or to those involved in making the statistical analyses.

The results of this study, in which the supplements were administered daily without interruption for six months, indicated according to standard statistical analyses as well the technique employing the Wetzel grid technique that when the treated groups were compared to the control group as a basis, 50 mg. daily doses of oxytetracycline provided the best growth promoting effects with +0.97 levels/month growth improvement rate, while daily doses of 1 Gm. of lysine provided + 0.64 levels/month, and daily doses of 10 mg. of oxytetracycline gave + 0.12 levels/month.

There were no toxic or untoward effects noted as a result of extended administration of these supplements. No instances of emergence of oxytetracycline resistant strains of *Staphylococcus aureus* were encountered.

Continued observations of these children lead to the conclusion that the effects of 50 mg. doses of oxytetracycline persist in their growth promoting effects a number of months after they have been discontinued. Thus, it would appear from the foregoing data that the addition of growth promoting supplements, particularly 50 mg. of oxytetracycline daily, to deficient tropical diets, may be the most economically practical way to correct simple growth failure in native tropical children.

The use of penicillin V, tetracycline, and prednisone in combined antibiotic-steroid treatment of infectious asthma in children was presented by Finke. Sixty-five children with infectious asthma were treated continuously with antibiotics for up to six years, and with anti-inflammatory steroids for as long as five years, were followed over an average period of four years. Disappearance or marked decrease of respiratory symptoms, sharp reduction of disabling respiratory illnesses, and considerable increase of vital capacity could be achieved in almost all cases. Recovery usually was most dramatic, complete, and lasting in early cases, but even in many children with longstanding, intractable asthma, prolonged treatment with antimicrobials and steroids restored the respiratory and general health.

In recent years, newer agents such as penicillin V, tetracycline, and prednisone have made this type of therapy safer,

more effective, and easier. Complications from these drugs were almost negligible in this series of children. Figures on vital capacity, acute respiratory illnesses, and absenteeism from school indicate a prompter therapeutic response than was observed with previous medications.

In this clinical study the combination of penicillin and tetracycline proved of particular value in shortening the initial treatment and preventing subsequent relapses. Once the infection was controlled, true allergic respiratory manifestations usually could be controlled by oral and local administration of prednisone alone, or in combination with antihistamines.

Clinical observations on the toxicity of tetracyclines in man with experimental studies in animals were discussed by Farhat, Schelhart, and Musselman of the University of Nebraska College of Medicine, Omaha. Finding of high serum levels of antibiotics in patients with renal disease or postoperative renal impairment led the authors to determine toxic serum levels of tetracyclines in experimental animals. Toxic doses of tetracycline antibiotics have been known, but to the authors' knowledge since the work of Sedwitz, Bateman, and Klopp the determination of toxic serum levels has not been undertaken.

High doses of tetracyclines (250 to 300 mg./Kg. body weight) were given intraperitoneally in divided doses to rabbits. Serum levels, blood NPN and BUN studies were done daily. It was noted that as the serum level of tetracyclines reached 20 to 40 micrograms per ml. the NPN and BUN began to rise. The elevation of serum level and NPN from this stage on was rapid and was followed by the death of the animals. The serum level just before death ranged between 160 and 320 micrograms per ml.

It is suggested that antibiotics be administered with caution to patients with impaired renal function. Elevation of the NPN in these patients suggests a raise in serum level of antibiotics.

Treatment of acne vulgaris with tetracycline-nystatin and tetracycline was reported by Robinson of the Farragut Medical Building, Washington, D. C. His paper discusses the role of broad-spectrum antibiotics in the over-all management of acne vulgaris and reports the results of oral antibiotic therapy in controlling the pustular component in 280 patients completing the prescribed treatment course. Tetracycline-nystatin was employed in 104 patients, and tetracycline in 176. No roentgen therapy or other definite therapeutic modality was used with the antibiotics. Infecting organisms were primarily *Staphylococcus aureus* and *Staphylococcus albus*. Dosage for each drug was one gram daily for a minimum of 30 days. As clearing occurred, dosage was reduced. Excellent or good therapeutic results were obtained in 58.7 percent of patients receiving tetracycline-nystatin, and in 60.2 percent of those receiving tetracycline. Toxic effects necessitated discontinuance of therapy in 6.7 percent of patients on tetracycline-nystatin, and in 9.0 percent of patients on tetracycline. In this series, patients who obtained an excellent result experienced no significant exacerbation following cessation of antibiotic therapy.

QUINOCYCLINE COMPLEX antibiotics were described by Celmer, Murai, Rao, Tanner and Marsh of the Research Laboratories of Chas. Pfizer and Co., Inc. Filtrates from a strain of *Streptomyces aureofaciens* have been shown to contain a unique group of related amphoteric antibiotics, termed the quinocycline complex. Solvent extraction of neutral broths led to the recovery of a brilliant yellow multiple-component solid which exhibited high *in vitro* activity against gram-positive and acid fast bacteria. Two highly active components of the complex, quinocycline-A and quinocycline-B, were characterized as relatively labile primary elaboration products. Invariably, isolates of these antibiotics contained substantial quantities of their more stable and less active respective isomers, isoquinocycline-A and isoquinocycline-B. Deparation of the various entities was accomplished by fractional crystallizations of appropriate salts and by cointercurrent distributions.

The ultimate interrelationship of the quinocycline complex was elucidated by acid hydrolysis studies. Quinocycline-A and quinocycline-B contain a common microbiologically-active chromophoric nucleus, *quinocycline*, and dissimilar polyol moieties, compound-A and compound-B, respectively. Significantly, the generic compound quinocycline readily isomerized, with considerable loss of potency, to more stable isoquinocycline which was identical with the common acid hydrolysis product of isoquinocycline-A and isoquinocycline-B.

Biologic studies on the quinocycline complex antibiotics were reported by McBride and English of the Bacteriology Laboratory, Pfizer Therapeutic Institute, Maywood, New Jersey. The original crude antibiotic complex was active in a range of 0.03 mcg./ml. to 0.07 mcg./ml. against pathogenic strains of *Mycobacterium tuberculosis* var. *hominis*. In addition, there was limited activity against a variety of gram-positive organisms including antibiotic resistant strains of *Micrococcus pyogenes* var. *aureus*.

In the process of the chemical characterization of this complex, a series of six closely inter-related antibiotics of varying activity was isolated. These active components were evaluated individually *in vitro* against several strains of pathogenic tubercle bacilli and selected components were also evaluated *in vivo*. *In vitro* spectra against a variety of bacterial species were obtained and in some cases, animal protection tests against experimental infections were carried out.

Some of the components were significantly more active than either streptomycin or isonicotinic acid hydrazide in an *in vitro* test. No evidence of synergism with known antituberculous agents was obtained. The components were found to exhibit a high order of toxicity for mice when administered on chronic basis. Although some members of the complex were able to offer significant protection to mice experimentally infected with tuberculosis, the chemotherapeutic index was very low.

VANCOMYCIN (Vancocin, Lilly) is an antibiotic obtained from a species of *Streptomyces orientalis*. Further studies on the purification of vancomycin were reported by Higgins, Harrison, Wild, Bungay, and McCormick of Eli Lilly Research Laboratories. Purified amorphous vancomycin hydrochloride preparations made by adsorption-desorption of Permutit DR, precipitation as the water-insoluble picrate, and conversion to the acetone-insoluble hydrochloride salt were deionized on a mixed bed ion exchange column. Concentration of the salt-free effluent led to the crystallization of the insoluble vancomycin free base. Subsequently, vancomycin-free base was crystallized directly from aqueous solutions and water-miscible organic solvents such as dimethylacetamide or dimethylsulfoxide. Analytical and physical data, known constituents, useful color tests, and *p*H stability of recrystallized vancomycin were reported.

LOS ANGELES

APHA & ASHP

► HOSPITAL PHARMACISTS from over the nation and representing the forty-eight affiliated chapters of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS will meet in Los Angeles for the 1958 Annual Meeting on April 20, 21 and 22. Meetings will be held in conjunction with the Convention of the American Pharmaceutical Association and affiliated organizations scheduled at the Biltmore Hotel during the week of April 20.

Members of the three ASHP affiliated chapters in California will actively participate in arrangements for the meetings with the Southern California Chapter of the ASHP in Los Angeles serving as host. A Steering Committee is responsible for coordinating the overall plans for ASHP events sponsored by the local chapter. This Committee includes Jack S. Heard, Chairman, ASHP Local Arrangements Committee; Joseph H. Beckerman, President, Southern California Society of Hospital Pharmacists; and Charles G. Towne, a member of the Executive Committee of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. Other hospital pharmacists serving on the overall committee include Nellie Nigro, University of California Hospital, Los Angeles; Melvin Schwartz, Mount Sinai Hospital, Los Angeles; John H. Plake, White Memorial Hospital, Los Angeles; Emily Alekna, Huntington Hospital, Los Angeles; R. C. Slanker, Los Angeles County Hospital, Los Angeles; Lillie Weil, Methodist Hospital, Arcadia; and Sidney Mogul, Veterans Administration Regional Office, Los Angeles.

The local group will also maintain a reception desk at registration and the ASHP will sponsor a suite of rooms where hospital pharmacists may meet for informal discussions throughout the week.

World Famed Wilshire Boulevard, Los Angeles

CONVENTION

APRIL 15 - 20

Business Sessions

In addition to the presentation of papers and entertainment scheduled during the Annual Meeting, the business of the SOCIETY will be conducted at the House of Delegates Session and two General Sessions. Also, the Executive Committee will meet on Saturday prior to the opening of the Annual Meeting.

The House of Delegates, which includes representatives of the affiliated chapters, the members of the Executive Committee and the Chairmen of Special Committees, will meet on Sunday afternoon at 2 P.M. The Address of the President-Elect, Robert C. Bogash, will be presented at that time. Other items of particular interest to delegates and members of affiliated chapters will be scheduled for this session.

Secretaries of ASHP affiliates will receive delegate forms and all chapters are urged to send representatives to the Annual Meeting.

Reports of officers and Committees, along with other SOCIETY business, will be conducted during the two General Sessions.

Program

The SOCIETY's Committee on Program and Public Relations, headed by Walter M. Frazier, Chief Pharmacist at Springfield City Hospital, Springfield, Ohio, has announced the program for the Annual Meeting. Other members of the Committee include: Herbert Flack, Jefferson Medical College Hospital, Philadelphia, Pa.; Jack Heard, University of California Medical Center, Los Angeles, Calif.; Louis Jeffrey, Albany Hospital, Albany, N. Y.; Russell Lovell, 476 Wirth Avenue, Akron, Ohio; Evlyn Gray Scott, St. Luke's Hospital, Cleveland, Ohio; William Tester,

Convention Headquarters, The Biltmore

University of California Hospital, Los Angeles

Mount Sinai Hospital

Wadsworth General Hospital—General Hospital Unit of the V.A. Center

Acute Unit, Los Angeles County General Hospital

University of Iowa Hospitals, Iowa City, Ia.; and John Webb, Massachusetts General Hospital, Boston, Mass.

The following papers have been scheduled for presentation during the general sessions on Monday and Tuesday:

"New Patterns of Hospital Pharmacy Service," by Grover C. Bowles, Jr., Chief Pharmacist, Baptist Memorial Hospital, Memphis, Tenn.

"Rational Drug Therapy," by Austin Smith, M.D., Editor, *Journal of the American Medical Association,* Chicago, Ill.

"Current Trends in Antibiotic Therapy," by William L. Hewitt, M.D., Associate Professor of Medicine, University of California Medical Center, Los Angeles, Calif.

"Participation of the Hospital Pharmacist in Teaching in the Nursing School Program," by Sister M. Gonzales, Chief Pharmacist, and Gerard Wolf, Assistant Chief Pharmacist, both at Mercy Hospital, Pittsburgh, Pa.

"Plastics and the U. S. P. Requirement for Airtight, Light-Resistant Containers," by George F. Archambault, Pharmacist Director, Chief, Pharmacy Branch, Division of Hospitals, Bureau of Medical Services, U. S. Public Health Service, Washington, D. C.

"Effectiveness of Enteric Coatings," by Orville Miller, Professor, School of Pharmacy, University of Southern California, Los Angeles, Calif.

"Improved Barium Sulfate Suspensions," by Joseph Beckerman, Assistant Chief Pharmacist, University of California Hospital, Los Angeles, Calif.

"Strip Packaging," by Robert Bogash, Director, Pharmacy Service, Lenox Hill Hospital, New York, N. Y.

"A Study of the Factors Influencing Drug Prices in the Los Angeles Area," by Gerald Kramer, North Glendale Memorial Hospital, North Glendale, Calif.

"A New Technique for the Preparation of Sterile Carcinogenic Pellets for Implantation in Experimental Animals," by Robert W. Case, Chief Cancer Research Pharmacist, Roswell Park Memorial Institute and Instructor, School of Pharmacy, University of Buffalo, Buffalo, N. Y.; Carl T. Brueckman, formerly Staff Pharmacist, Roswell Memorial Institute and presently with U. S. Army Medical Service Corps, Fort Sam Houston, Tex.; and Clifton J. Lord, Assistant Professor and Director, Hospital Pharmacy Division, School of Pharmacy, University of Buffalo, Buffalo, N. Y.

"Development of Research in Hospital Pharmacy," by Glenn L. Jenkins, Dean, Purdue University School of Pharmacy, Lafayette, Ind.

"Current Trends in Germicides," by Carl A. Lawrence, Director, Bureau of Laboratories, Los Angeles County Health Department, and Assistant Clinical Professor of Infectious Diseases, University of California Medical Center, Los Angeles, Calif.

"Survey Technics and the Audit," by Don E. Francke, Chief Pharmacist, University Hospital, and Clifton J. Latiolais, Assistant Program Director, Audit of Pharmaceutical Service in Hospitals, both of Ann Arbor, Mich.

"Application and Use of the American Hospital Formulary Service," by William Heller, Chief Pharmacist, University of Arkansas Hospital, Little Rock, Ark.

"Poison Control Centers," Panel Discussion: *Moderator,* H. Louis Verhulst, Assistant Director, National Clearinghouse for Poison Control Centers, Department of Health, Education and Welfare, Washington, D. C.

Participants, Clara Henry, Oakland Hospital, Oakland, Calif.; Wendell Hill, Orange County Memorial Hospital, Orange, Calif.; Albert Picchioni, Professor of Pharmacology, University of Arizona, School of Pharmacy, Tucson, Ariz. and Robert Simons, Delaware Memorial Hospital, Wilmington, Del.

"Requirements for the Establishment of Hospital Pharmacy Internships and the Accreditation Program," by Paul F. Parker, Director, Division of Hospital Pharmacy, American Pharmaceutical Association, Washington, D. C.

"Chapter Publications," by Louis Jeffrey, Chief Pharmacist, Albany Hospital, Albany, N. Y.

"Role of an Antibiotics' Committee of the Medical Staff," by Sister M. Rebecca, Chief Pharmacist, St. Benedict's Hospital, Ogden, Utah.

"Effect of Plastics on Parenteral Products—I. Compatibility Studies of Plastic Syringes with Parenteral Products," by C. N. Dhorda, Graduate Student, and J. Autian, Assistant Professor of Pharmacy, both at University of Michigan, College of Pharmacy, Ann Arbor, Mich.

"The Necessity for a Bulk-Compounding Formula Compendium for Hospital Pharmacists," by Clifton F. Lord, Assistant Professor of Pharmacy and Director, Division of Hospital Pharmacy, School of Pharmacy, University of Buffalo; and Robert W. Case, Chief Cancer Research Pharmacist, Roswell Park Memorial Institute, and Instructor, School of Pharmacy, University of Buffalo, both of Buffalo, N. Y.

"A New Concept in Labeling for Large and Small

Disneyland from Square

Hollywood Freeway

Oranges and snow in San Gabriel Valley

San Fernando Mission, Founded 1797

Hospitals," by Herbert L. Flack, Director, Pharmacy Service; and Fred G. Salfie, Pharmacy Resident, both at Jefferson Medical College Hospital, Philadelphia, Pa.

Seminar on Education and Training

A pre-convention Seminar on Hospital Pharmacy Education and Training is scheduled for Saturday night, April 19 at the Headquarters Hotel. This event is being held in accordance with a resolution passed at the 1957 Annual Meeting and President Godley has appointed Herbert L. Flack, Jefferson Medical College Hospital, Philadelphia, and Charles G. Towne, Veterans Administration Center, Los Angeles, to serve as co-chairmen for the Seminar. This special session is intended to offer educators, hospital pharmacy practitioners, students, and interns an opportunity to discuss the various aspects of education and training provided in this specialty.

Subjects to be covered in the Seminar include: Recruitment of Hospital Pharmacists, The Hospital Pharmacy Curricula, The Viewpoint of Hospital Administration on Training Programs for Career Hospital Pharmacists, Elective Courses Available for Students Preparing for Hospital Pharmacy Practice, Internship and Residency Programs, and Current Research in Graduate Programs.

Special Events

Working in cooperation with the national group, the local committee has arranged for a number of special events for hospital pharmacists attending the Annual Meeting. On Sunday evening the Southern California Chapter will sponsor a social hour immediately following the meeting of the House of Delegates. This will be an informal "get-together" when all members attending the Annual Meeting will have an opportunity to meet the local group as well as officers of the ASHP.

A highlight of the special events will be the 1958 H. A. K. Whitney Award Lecture which will be held at the Los Angeles Athletic Club on Monday night. This Award, established by the Michigan Society of Hospital Pharmacists in honor of the first Chairman of the Society, is given annually to an individual who has made outstanding contributions in the field of hospital pharmacy. The 1958 recipient is Mr. Walter M. Frazier, Chief Pharmacist at Springfield City Hospital, Springfield, Ohio. This event holds particular significance this year due to the recent death of Mr. H. A. K. Whitney, in whose honor the Award was established.

The traditional breakfast for hospital pharmacists will be held on Tuesday morning at the Headquarters Hotel.

Tribute to Spease and Whitney

During the 1958 Annual Meeting a special tribute will be paid to two recently deceased honorary members of the Society—Edward Spease and Harvey A. K. Whitney. Both of these men were well known to hospital pharmacists for their contributions to the specialty of hospital pharmacy as well as the profession.

A.Ph.A. Activities

The official opening of the Convention of the American Pharmaceutical Association will take place on Sunday night, April 20. Affiliated organizations, including the National Conference of State Pharmaceutical Association Secretaries, the American Association of Colleges of Pharmacy, the American College of Apothecaries, and the ASHP, will meet from Saturday, April 19, through Tuesday, April 22. The A.Ph.A.'s business meeting will open with the First General Session on Tuesday night.

Dr. Alvah G. Hall, Dean of the College of Pharmacy of the University of Southern California, has accepted the honorary chairmanship of the Los Angeles Convention Committee. Mr. Ben Kingwell has been appointed General Chairman of the Convention Committee, and Dr. Orville Miller will function as Secretary of the Committee. Mr. Henry Henley, Vice-President of McKesson & Robbins and Mr. Roy V. Schwab, President of Brunswig Drug Co., Los Angeles, will be Co-Chairmen of the Finance Committee.

The management of the A.Ph.A. Convention is under the direction of Dr. Robert P. Fischelis, Secretary and General Manager of the American Pharmaceutical Association, who has announced the appointment of Mr. George B. Griffenhagen as Deputy Director and Coordinator of Convention Activities. Mr. Griffenhagen has been associated with Dr. Fischelis in the management of the A.Ph.A. convention since the Centennial meeting in Philadelphia in 1952. More recently he functioned as Secretary General of the 4th Pan-American Congress of Pharmacy and Biochemistry held in Washington last November.

Mr. Griffenhagen is a former resident of the Los Angeles area and a graduate of the College of Pharmacy of the University of Southern California where he was also a member of the faculty for several years.

In addition to the direct bulletin covering various details of the Convention which will be sent to each member of the A.Ph.A. by mail in the near future, a complete tentative program of the Convention will appear in the March issue of the *Practical Pharmacy Edition of the Journal of the American Pharmaceutical Association.*

FIRST AID MEASURES FOR POISONING

Recommendations of Committee on Toxicology

The following recommendations on first-aid measures for poisoning have been adopted by the Committee on Toxicology. These recommendations are made in response to numerous requests to the American Medical Association for general instructions for poisoning emergencies. They are intended for use in educating the public in what to do when poisoning occurs.*— BERNARD E. CONLEY, PH.D., *Secretary, Committee on Toxicology.

Emergency Telephone Numbers

Physician_____ Fire Dept._____

Hospital_____ (resuscitator)

Pharmacist_____ Police_____

Rescue Squads _____

The aim of first-aid measures is to help prevent absorption of the poison. SPEED is essential. First-aid measures must be started at once. If possible, one person should begin treatment while another calls a physician. When this is not possible, the nature of the poison will determine whether to call a physician first or begin first-aid measures and then notify a physician. Save the poison container and material itself if any remains. If the poison is not known, save a sample of the vomitus.

Measures To Be Taken Before Arrival of Physician

I. Swallowed Poisons

Many products used in and around the home, although not labeled "poison," may be dangerous if taken internally. For example, some medications which are beneficial when used correctly may endanger life if used improperly or in excessive amounts.

In all cases, *except those indicated below,* REMOVE POISON FROM PATIENT'S STOMACH IMMEDIATELY by inducing vomiting. This cannot be overemphasized, for it is the essence of the treatment and is often a lifesaving procedure. Prevent chilling by wrapping patient in blankets if necessary. Do not give alcohol in any form.

A. Do Not Induce Vomiting If:

1. Patient is in coma or unconscious.
2. Patient is in convulsions.
3. Patient has swallowed petroleum products (i.e., kerosene, gasoline, lighter fluid).
4. Patient has swallowed a corrosive poison (symptoms: severe pain, burning sensation in mouth and throat, vomiting).
   CALL PHYSICIAN IMMEDIATELY
   (a) Acid and acid-like corrosives: sodium acid sulfate (toilet bowl cleaners), acetic acid (glacial), sulfuric acid, nitric acid, oxalic acid, hydrofluoric acid (rust removers), iodine, silver nitrate (styptic pencil).
   (b) Alkali corrosives; sodium hydroxide lye (drain cleaners), sodium carbonate (washing soda), ammonia water, sodium hypochlorite (household bleach).

If the patient can swallow after ingesting a *corrosive poison,* the following substances (and amounts) may be given:

For acids: milk, water, or milk of magnesia (1 tablespoon to 1 cup of water).

For alkalis: milk, water, any fruit juice, or vinegar.

For patient 1-5 years old—1 to 2 cups.

For patient 5 years and older—up to 1 quart.

B. Induce Vomiting When Non-corrosive Substances Have Been Swallowed:

1. Give milk or water (for patient 1-5 years old—1 to 2 cups; for patient over 5 years—up to 1 quart).
2. Induce vomiting by placing the blunt end of a spoon or your finger at the back of the patient's throat, or by use of this emetic—2 tablespoons of salt in a glass of warm water.

When retching and vomiting begin, place patient face down with head lower than hips. This prevents vomitus from entering the lungs and causing further damage.

II. Inhaled Poisons

1. Carry patient (do not let him walk) to fresh air immediately.
2. Open all doors and windows.
3. Loosen all tight clothing.
4. Apply artificial respiration if breathing has stopped or is irregular.
5. Prevent chilling (wrap patient in blankets).
6. Keep patient as quiet as possible.
7. If patient is convulsing, keep him in bed in a semi-dark room; avoid jarring or noise.
8. Do not give alcohol in any form.

III. Skin Contamination

1. Drench skin with water (shower, hose, faucet).
2. Apply stream of water on skin while removing clothing.
3. Cleanse skin thoroughly with water; rapidity in washing is most important in reducing extent of injury.

IV. Eye Contamination

1. Hold eyelids open, wash eyes with gentle stream of running water *immediately.* Delay of few seconds greatly increases extent of injury.
2. Continue washing until physician arrives.
3. *Do not use chemicals;* they may increase extent of injury.

V. Injected Poisons (scorpion and snake bites):

1. Make patient lie down as soon as possible.
2. Do not give alcohol in any form.
3. Apply tourniquet above injection site (e.g., between arm or leg and heart). The pulse in vessels below the tourniquet should not disappear, nor should the tourniquet produce a throbbing sensation. Tourniquet should be loosened for 1 minute every 15 minutes.
4. Apply ice-pack to the site of the bite.
5. Carry patient to physician or hospital; DO NOT LET HIM WALK.

VI. Chemical Burns

1. Wash with large quantities of running water (except those caused by phosphorus).
2. Immediately cover with loosely applied clean cloth.
3. Avoid use of ointments, greases, powders, and other drugs in first-aid treatment of burns.
4. Treat shock by keeping patient flat, keeping him warm, and reassuring him until arrival of physician.

Measures to Prevent Poisoning Accidents

A. Keep all drugs, poisonous substances, and household chemicals out of the reach of children.

B. Do not store nonedible products on shelves used for storing food.

C. Keep all poisonous substances in their original containers; do not transfer to unlabeled containers.

D. When medicines are discarded, destroy them. Do not throw them where they might be reached by children or pets.

E. When giving flavored and/or brightly colored medicine to children, *always* refer to it as medicine—*never* as candy.

F. Do not take or give medicine in the dark.

G. *READ LABELS* before using chemical products.

J.A.M.A. 165:686 (Oct. 12) 1957

TURBIDIMETRIC ASSAY

for

BENZALKONIUM CHLORIDE

by RUSSELL A. POST and ORVILLE H. MILLER

► THE EXTENSIVE USE OF BENZALKONIUM CHLORIDE (BAK) in germicidal solutions prepared in the hospital pharmacy indicates a need for simple and rapid quantitative assay for this type of product. In order to be of most value, the assay procedure should be applicable to concentrations as low as 0.0025 percent and should be unaffected by variations in *p*H, temperature, and added chemicals.

Presently available methods for assaying BAK solutions are generally too elaborate and time consuming for use in the hospital pharmacy where relatively small lots of a variety of concentrations are prepared.

Dubois[1] has stated that all methods of assay for quaternary ammonium germicides currently in use are based on the interaction between the high molecular weight cations and various anions to form salts or complexes. The particular procedure is dependent upon the properties of the salt, such as its solubility in water and organic solvents, color, etc.

A number of titrimetric and colorimetric methods are available for the determination of BAK in solutions. These methods have been reviewed by Dubois[1] and Lawrence.[2]

The present U.S.P. assay developed by Auerbach[3] consists of precipitation with ferricyanide, filtration, addition of potassium iodide, and titration of the liberated iodine. These methods are applicable to small concentrations but due to the cumbersome manipulation procedures, time required or unstable reagents, their usefulness for assaying small lots is limited.

Various test-paper methods have been devised which are simple and rapid but not highly accurate. These papers, impregnated with a dye, are immerged in a solution of the quaternary ammonium germicide being

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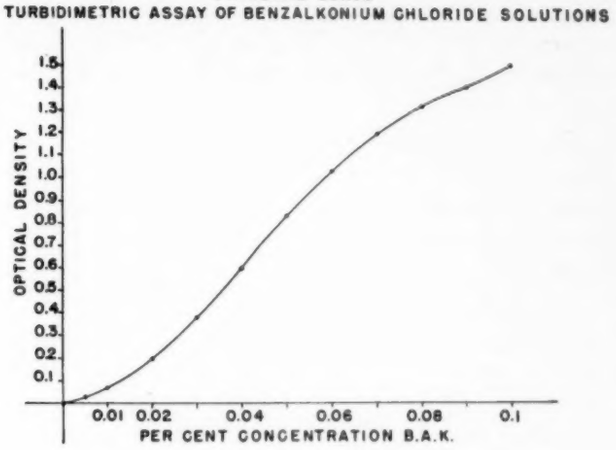
FIG. 1
STANDARD CURVE
TURBIDIMETRIC ASSAY OF BENZALKONIUM CHLORIDE SOLUTIONS



tested. The concentration is determined by comparing the color produced with a color chart. These tests have proved of value in field work.[2]

The fact that an insoluble salt is formed by the reaction of quaternary ammonium germicides and many anionic substances has indicated the possibility of devising a simple turbidimetric assay. Suitable colorimetric or spectrophotometric equipment adaptable to turbidimetric assays is generally available in the hospital clinical laboratory. Gain and Lawrence[4] have described a rapid assay procedure utilizing normal horse serum as the precipitating agent.

Flanagan, Drennen, and Goetchius[5] have devised a turbidimetric method utilizing a solution of the sodium salt of a condensed aryl sulfonic acid as the precipitating agent. Both of these methods while quite rapid, have a limited range and limited accuracy. In the last method an excess of reagent tended to solubilize the precipitates first formed.

Experimental

There are many other possible precipitation reactions between quaternary ammonium germicides and various anionic substances. BAK solutions were combined with a number of such substances at low dilutions in a search for a precipitant that would be applicable to concentrations as low as 0.0025 percent (1:40,000). This is the lowest concentration normally utilized in a hospital.

Of a number of substances giving visible precipitation at 1:40,000, sodium salicylate was selected as the preferred precipitant on the basis of its ready availability, lack of color, stability, and in particular because of the nature of the precipitate produced. This precipitate remains finely dispersed with no evidence of coagulation or settling after standing several hours. Furthermore, the amount of precipitate formed was not affected by a large excess of sodium salicylate. Methylcellulose can be added to further assure stability of the precipitate.

Reagents. (a) Standard BAK solution. Determine the potency of the usual 12.8 percent commercial solution using the U.S.P. assay. From this solution prepare appropriate dilutions in the range to be compared. (b) Salicylate reagent, sodium salicylate 0.5 percent plus methylcellulose 2500, 0.5 percent in distilled water.

Procedure. Dilute sample, if necessary, to concentration of 0.0025 percent—0.05 percent (1:40,000-1:2,000). To 5 ml. of sample add 5 ml. of salicylate reagent and mix. After ten minutes determine loss of transmitted light in any suitable photocolorimeter or spectrophotometer using a blue filter or 450 m μ. Use reagent blank (5 ml. water plus 5 ml. salicylate reagent) for adjusting instrument. An optical density or similar log scale is preferable as readings will be directly proportional to concentration. Determine concentration by comparison with standard of approximately same concentration or with standard curve previously prepared using a series of standard solutions covering desired concentration range.

Fig. 1 shows a standard curve prepared from such a series of standards using a Beckman DU Spectrophotometer with readings in optical density.

Effect of Time Upon Optical Density. The effect of ageing on the precipitate was determined at concentrations of 0.05 percent and 0.01 percent. The optical density was determined at time intervals from one-half to one hundred and twenty minutes. There was a small increase in optical density for the first

ten minutes with no further change up to one hour. After one hour there was a slight decrease. The results appear in Fig. 2. On this basis the optical density should preferably be determined at a ten to sixty minute interval after precipitation.

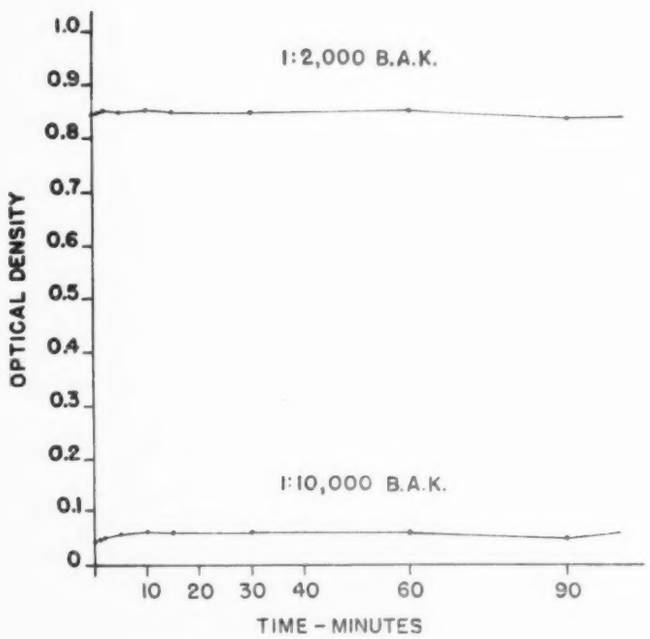
Effect of Order of Mixing. At the lower concentrations slightly higher optical density was obtained upon adding the reagent to the sample as compared to adding the sample to the reagent. No detectable difference was noted at the 0.05 percent concentration.

Effect of Temperature and *p*H. No difference in optical density was observed at concentrations of 0.01 percent and 0.05 percent over the temperature range 15-30°C.

BAK is often combined with alkaline materials such as sodium bicarbonate and sodium carbonate. Therefore, the effect of *p*H upon the optical density was studied. No effect was noted over the *p*H range 5.0 to 10.5 (½ percent sodium carbonate). In more acidic solutions the optical density increased probably due to the precipitation of free salicylic acid.

Effect of Other Substances. BAK solutions often contain other substances such as sodium nitrite, phosphate buffers, alcohols and dyes, particularly D&C Red No. 39. The sodium nitrite and phosphate buffers had no effect upon the optical density. Ethyl and isopropyl alcohol produced a decrease in optical density particularly at high concentrations. However, the usual 1:1,000 BAK tincture containing 50 percent alcohol can be assayed by tenfold dilution to give 0.01 percent BAK and 5 percent alcohol. At these concentrations there is no change in optical density as compared to non-alcoholic solutions.

FIG. 2
EFFECT OF TIME ON THE TURBIDIMETRIC ASSAY OF BENZALKONIUM CHLORIDE SOLUTION



Solutions containing D&C Red No. 39 were successfully assayed using a red filter of 700mμ. Using red light substantially reduces the optical density but largely eliminates interference by the dye. In this case the reagent blank should consist of 5 ml. of sample containing the dye plus 5 ml. of methylcellulose solution 0.5 percent. If other dyes are present, a similar reagent blank should be used but the filter or wave length should be selected so as to give minimum light absorption by the dye.

Accuracy of Method. The unusual stability of the BAK-salicylate precipitate permits an accuracy approaching that of colorimetric methods. The ultimate accuracy depends upon the concentration and the limitations of the particular instrument used.

Application to Other Quaternary Ammonium Germicides. A similar precipitate was obtained with benzethonium chloride solution but not with cetylpyridinium chloride or cetyl-trimethyl ammonium bromide solutions.

Summary

1. A simple turbidimetric assay for benzalkonium chloride solutions based on precipitation with salicylate is proposed. The method is applicable to concentrations ranging from 0.0025 to 0.05 percent.

2. The effect of time, temperature, *p*H, and the presence of certain substances often found in BAK solutions was determined.

3. The unusual stability of the benzalkonium-salicylate precipitate permits an accuracy approaching that of colorimetric methods.

4. The method also appears applicable to benzethonium chloride but not to cetylpyridinium chloride or cetyl-trimethyl ammonium bromide.

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Therapeutic Trends

edited by WILLIAM JOHNSON

Bemegride—In Terminating Barbiturate Anesthesia

The results of a clinical trial of bemegride in terminating barbiturate anesthesia are reported by Wyke *et al* in *Lancet* 2:1025 (Nov. 23) 1957. Bemegride accelerates considerably the recovery of respiratory function, corneal reflexes, and oropharyngeal and somatic reflex responses. It has little specific effect on full recovery of consciousness, although it does diminish the depth of unconsciousness. Toxic effects of bemegride are rare with the doses required to produce these effects. This drug appears to act primarily as a stimulant to the reticular nuclei of the brain-stem. Bemegride (β-ethyl-β-methylglutarimide) reverses, to a large extent, the narcotic effects of barbiturates. It is used widely in barbiturate poisoning to counteract the narcotic action of these drugs, usually with considerable success.

Vitamin B_1—In Auditory Damage by Streptomycin

Twenty-nine cases of pulmonary tuberculosis were observed in which intoxication with streptomycin (dihydrostreptomycin or combined streptomycins) had occurred. In 10 of these cases impaired hearing developed after administration of 2 to 10 Gm. of streptomycin, indicating idiosyncrasy. Fifteen cases were favorably treated with daily intravenous administration of fortified vitamin B_1, 100 mg. The audiograms of seven cases are presented. Early detection and treatment are recommended because of difficulty in treating advanced impairment even though the audiogram shows only slight abnormality. Prophylaxis using fortified vitamin B_1 100 mg. is suggested at the time of administration of streptomycin with repetition the following day. After a two-year study, Ozaki reports a steady decrease in the number of patients with impaired hearing after therapeutic regimens of streptomycins. The results of this study are to be found in *A.M.A. Arch. Otolaryng.* 66:673 (Dec.) 1957.

W-1548—A Carbonic Anhydrase Inhibitor

W-1548 is a potent oral diuretic agent of the carbonic-anhydrase-inhibitor type. Side effects and toxicity are negligible in dosage up to 2 Gm. a day. The drug is best prescribed on an intermittent regimen to prevent refractoriness to the drug and to elicit its fullest diuretic effect. Although it was originally intended as a drug for cardiac edema, its diuretic effect in 4 out of 5 cases of Laennec's cirrhosis suggests that its usefulness in this disease be further investigated. Although W-1548 does not relieve many refractory edemas when used alone, in conjunction with other therapeutic agents it often contributes the additional factor that makes the difference between cardiac compensation and decompensation. This study is reported in *New Eng. J. Med.* 257:1074 (Nov. 28) 1957. W-1548 (p-sulfamyl-2-hydroxy-ethyl-carbanilate) was supplied by Warner-Chilcott Laboratories.

Penicillamine—In Treatment of Metal Poisoning

The chelating agent penicillamine (β,β,-dimethyl cysteine) was first introduced as a treatment for Wilson's disease. It is effective when given by mouth and high dosages may apparently be given for a long period with safety. Boulding and Baker report in *Lancet* 2:985 (Nov. 16) 1957 on the use of penicillamine in two cases of lead poisoning, one of hemosiderosis and one of hemochromatosis. Evidence suggests that penicillamine may be of use in the therapy of metal intoxications other than hepatolenticular degeneration. Further investigations are warranted because of its apparent ability to produce rapid diuresis of copper, lead, and iron in poisoning with these metals.

Glutamine—In Treatment of Peptic Ulcers

In a preliminary study of 57 patients on the evaluation of glutamine in the treatment of peptic ulcer, an initial group of 12 patients treated with conventional therapy was given a glutamine supplement at the outset and at various times after conventional therapy was begun. Ten of this group continued glutamine therapy beyond twelve days, and the ulcers of 8 of the patients were healed by the first or second radiological reexamination at 2 or 4 weeks, respectively. Of 24 patients treated with glutamine alone, the ulcers of 12 healed by the first radiological reexamination at 2 weeks and the ulcers of 8 more patients healed by the second reexamination in approximately 4 weeks. Glutamine is a factor isolated

from cabbage juice. It is postulated that the inability of some investigators to duplicate previous results might be attributed to variation in the amount of glutamine in the juices of different cabbages. The results of this study by Shive *et al* appear in *Texas State J. Med. 53*:830 (Nov.) 1957. The glutamine for this study was supplied by the Merck Sharp and Dohme Division of Merck and Co.

Buthalitone—A Short-Acting Barbiturate

A thiobarbiturate, buthalitone, is evaluated by Simmons and Blanshard as an anesthetic agent for outpatient administration and the results are reported in *Brit. Med. J.* p. 1348 (Dec. 7) 1957. The results of this clinical trial indicate that buthalitone, as employed and evaluated, does not appear to be an advance in outpatient anesthesia. Thiopentone is used by these workers as the standard of comparison and it had been reported previously that recovery from buthalitone anesthesia was much more rapid than with thiopentone anesthesia. This present series does not corroborate this finding. Hiccup is a frequent and troublesome sequel to induction. It marred smooth induction and hampered manipulative surgery. Buthalitone has certain properties which make these workers prefer present available techniques and agents. Buthalitone sodium is the sodium salt of 5-allyl-5-(methylpropyl) thiobarbituric acid. It is a yellow powder which is readily soluble in water giving an extremely alkaline solution which is said to be unstable. The therapeutic index for mice has been shown to be the same as that of thiopentone.

UX-6—A Diuretic Agent

The experimental compound UX-6 (2-amino-4-isoamylamino-S-triazine hydrochloride) was observed for diuretic effectiveness in unhydrated dogs. There was significant increase in sodium, potassium, and water excretion. In contrast to currently available diuretics that are used clinically, there was a parallel increase in sodium and water excretion without a significant increase in the concentration of sodium in the urine. Bioassay studies were done in patients with mild congestive heart failure under controlled conditions on a metabolic ward. The results of these studies are tabulated. Dosages of more than 400 mg. per day did not increase the degree of diuresis. Side effects with doses of 400 mg. per day were usually mild to moderate, lasting one or two weeks and consisted of anorexia, nausea, fatigue, weakness, and drowsiness. Seventy-three percent of the patients experienced side effects. The results of this study by Moyer *et al* appears in *Antibiot. Med. Clin. Ther. 4*:685 (Nov.) 1957. It is concluded that UX-6 is not as effective as acetazoleamide or chlormerodrin in the control of congestive heart failure. The exact mechanism by which UX-6 produces diuresis is not known. The UX-6 for this study was supplied by U. S. Vitamin Corp., Arlington-Funk Laboratories Division.

Prednisolone—In Treatment of Tuberculosis

Preliminary results of treatment in a controlled trial are reported in which 46 patients were treated with chemotherapy alone and 44 treated with identical chemotherapy plus prednisolone. Clinical improvement was more rapid, especially in those who were acutely ill, in those treated with prednisolone, and there was a more rapid fall in the erythrocyte sedimentation rate in this group. Radiological improvement was significantly hastened by prednisolone over a six-months period, most of the significant difference occurring in the first two months. Cavity closure and sputum conversion were slightly hastened by prednisolone, but not to a significant degree. No patients receiving prednisolone showed evidence of deterioration, though a "rebound" phenomenon was observed radiologically in one-sixth of the cases. No serious side effects were recorded. The results of this study as a preliminary report of the Research Committee of the Tuberculosis Society of Scotland is to be found in *Brit. Med. J.* p.5054 (Nov. 16) 1957.

Triethylenephosphoramide—in Melanoma

Triethylenephosphoramide (TEPA) or the more stable compound triethylenethiophosphoramide (thioTEPA) was used to treat 13 out of 15 consecutive cases of widespread, disseminated, malignant melanoma. The initial course of treatment was generally given over a 10-20 day period. Following an initial test dose of 5 mg. of one of the drugs, use of a single daily intramuscular dose averaging 10 mg. was instituted. In some cases the drug was also given orally or intravenously. Predictable marrow depression occurred after approximately 2 weeks of therapy. The effective dose averaged 150 mg., with a range of 135 to 180 mg. Clinical experience with thioTEPA was not as satisfactory as with TEPA.

Treatment with TEPA or thioTEPA was given until a decrease occurred in the leucocyte count or platelet count. A leucocyte count of about 2,000 per cubic millimeter and a platelet count of 50,000 to 100,000 per cubic millimeter were achieved in all but two patients. The treatment did not save patients near death, but in two well-advanced cases all evidence of the disease disappeared at least temporarily.

The report on the use of TEPA and thioTEPA is contained in *J.A.M.A. 166*:37 (Jan. 4) 1958. The drugs were supplied by the Clinical Research Section of Lederle Laboratories.

Timely Drugs

Aristocort

COMPOSITION: Scored tablets containing 2 mg. (pink) or 4 mg. (white) triamcinolone.

INDICATIONS: Biosynthetic corticosteroid with enhanced glucocorticoid and markedly diminished mineralocorticoid characteristics; indicated in rheumatoid arthritis, respiratory allergy, inflammatory and allergic skin diseases, disseminated lupus erythematosus, nephrotic syndrome, pulmonary emphysema and fibrosis, and neoplastic diseases.

SIDE EFFECTS AND CONTRAINDICATIONS: Virtually none of major side effects, and fewer of the minor side effects, usually produced by corticosteroids; however, all traditional contraindications to long-term corticosteroid therapy should be observed.

DOSAGE: Generally one-third less than prednisolone, depending on condition being treated; total daily dose is divided into 4 doses and given with meals and at bedtime; maintenance level is reached by reduction of total daily dose in decrements of 2 mg. every 3 days; discontinuance of therapy must not be sudden, but should be carried out gradually over a period of as much as several weeks.

PACKAGING: Bottles of 30 tablets.

SUPPLIER: Lederle Laboratories.

Cardrase

COMPOSITION: Tablets containing 0.125 Gm. ethoxzolamide (6-ethoxybenzothiazole-2-sulfonamide).

INDICATIONS: Non-mercurial diuretic in mild to moderate congestive heart failure; effect achieved through inhibition of the enzyme carbonic anhydrase.

DOSAGE: In mild to moderate congestive heart failure, 62.5 to 125 mg. in the morning after breakfast for 3 consecutive days of each week, or on alternate days; in glaucoma, 62.5 to 250 mg. repeated 2 to 4 times daily depending on individual response in intra-ocular tension.

PACKAGING: Bottles of 25, 100, 1,000, and 5,000 tablets.

SUPPLIER: Upjohn Co.

Dartal

COMPOSITION: Tablets containing 5 mg. (white) or 10 mg. (peach) thiopropazate dihydrochloride.

INDICATIONS: Tranquilizer without sedation; controls excessive psychomotor and emotional activities associated with such disorders as agitated and anxiety states of insomnia, anorexia, abnormal excitement, etc.

SIDE EFFECTS AND CONTRAINDICATIONS: Extrapyramidal activity of pseudoparkinsonism, controlled by reducing or discontinuing therapy or by concurrently administering antiparkinson drugs, may occur on high dosages.

DOSAGE: For anxiety tension states, psychosomatic disorders and other neuroses, 5 mg. three times daily; for psychotic conditions, 10 mg. three times daily.

PACKAGING: Bottles of 50 and 500 tablets.

SUPPLIER: G. D. Searle & Co.

Diuril

COMPOSITION: Scored tablets containing 0.5 Gm. chlorothiazide.

INDICATIONS: Oral diuretic for initiation of diuresis and for prolonged daily maintenance of diuresis.

SIDE EFFECTS AND CONTRAINDICATIONS: Fluid and electrolyte imbalance may result from improper dosage and administration; dizziness and paresthesias reported as rare side effects.

DOSAGE: 0.5 or 1 Gm., once or twice daily; onset of effect within 2 hours, maximum effect usually in 4 hours, duration of effect 6 to 12 hours.

PACKAGING: Bottles of 100 and 1,000 tablets.

SUPPLIER: Merck Sharp & Dohme.

Liquamar

COMPOSITION: Scored tablets containing 3 mg. phenprocoumon [3-1'-(phenylpropyl)-4-hydroxycoumarin].

INDICATIONS: Anticoagulant in prophylaxis and treatment of thrombosis and embolism, including thrombophlebitis, phlebothrombosis, coronary thrombosis and pulmonary embolism.

SIDE EFFECTS AND CONTRAINDICATIONS: Usual contraindications for coumarin therapy; hemorrhagic sequellae may be controlled by increasing the blood prothrombin level with intravenous vitamin K_1

DOSAGE: 18 to 21 mg. the first day, 9 to 12 mg. the second day, 6 to 9 mg. the third day, and 0.75 to 4.5 mg. maintenance dose, is suggested.

PACKAGING: Bottles of 100 and 1,000 tablets.

SUPPLIER: Organon Inc.

Midicel

COMPOSITION: Quarter-scored tablets containing 0.5 Gm. sulfamethoxypyridazine.

INDICATIONS: Many gram-negative and gram-positive bacterial infections; particularly useful in infections of the urinary tract; moderately acetylated and slowly excreted by the kidneys.

DOSAGE: Initially, 1 Gm., followed by 0.5 Gm. daily thereafter, or 1 Gm. every other day for mild or moderate infections; for severe infections, initial dose of 2 Gm., followed by 0.5 Gm. daily, is recommended; children's dosage is calculated according to weight. Adequate fluid intake should be maintained during therapy and for 24 to 48 hours after treatment.

PACKAGING: Bottles of 24 and 100 tablets.

SUPPLIER: Parke, Davis & Co.

Neutrapen

COMPOSITION: Single dose vials containing 800,000 units of purified penicillinase (Neutrapen) as lyophilized powder.

INDICATIONS: Specific for penicillin reactions; an enzyme, it catalyzes the hydrolysis of penicillin to penicilloic acid, which is nonallergenic; indicated in all cases of penicillin reaction except immediate type of anaphylactic reaction.

SIDE EFFECTS AND CONTRAINDICATIONS: Some transient soreness at site of injection, which may be accompanied by erythema and local edema; intravenous use has been reported to cause chills and fever in some cases; should not be given concurrently with therapeutic administration of penicillin because it would destroy the penicillin.

DOSAGE: 800,000 U. injected intramuscularly as soon as possible after signs and symptoms of penicillin reaction appear; if necessary, dosage may be repeated at 3 to 4 day intervals; a third dose is rarely required. In anaphylactic reactions 800,000 U. should be given intravenously immediately, followed by 800,000 U. intramuscularly.

PACKAGING: 800,000 U. vials to be reconstituted with 2 ml. sterile distilled water; solution must be refrigerated and retains potency for one week.

SUPPLIER: SchenLabs Pharmaceuticals, Inc.

Paral

COMPOSITION: Ampuls, 2 ml., 5 ml. or 10 ml. of paraldehyde.

INDICATIONS: Sedative and hypnotic.

SIDE EFFECTS AND CONTRAINDICATIONS: May be contraindicated in broncho-pulmonary disease or hepatic insufficiency.

DOSAGE: May be diluted with sterile normal saline to a 10 percent solution for intravenous use, or 1 ml. may be injected very slowly undiluted.

PACKAGING: Boxes of 12 and 25 ampuls.

SUPPLIER: Testagar & Co.

Quiactin

COMPOSITION: Tablets containing 0.4 Gm. oxanamide.

INDICATIONS: Tranquilizer; modifies central nervous system activity, producing a calm, quieting effect lasting from 3 to 4 hours; mental alertness is not dulled, nor is drowsiness a problem.

DOSAGE: As quieting or tranquilizing agent, 0.4 Gm. 4 times daily.

PACKAGING: Bottles of 50 tablets.

SUPPLIER: Wm. S. Merrell Co.

Ritalin Injectable

COMPOSITION: Multiple dose vials containing 100 mg. methylphenidate hydrochloride and 100 mg. lactose in lyophilized form.

INDICATIONS: Central nervous system stimulant for use in oral surgery, respiratory depression, and psychiatric treatment; unlike oral Ritalin, the parenteral form has a much greater speed of action, and raises the severely lowered blood pressure of patients suffering from acute overdosage of barbiturates.

DOSAGE: In acute overdosage of barbiturates, 30 to 50 mg., repeated every 30 minutes; for lethargy induced by drugs, a daily total of 30 mg.; for psychiatric conditions associated with depression, 10 to 20 mg.

PACKAGING: Multiple dose vials of 100 mg., together with 10 ml. vials of sterile solvent containing 0.5% chlorobutanol, 0.5% citric acid, 0.5% sodium citrate, and 1% propylene glycol in water.

SUPPLIER: Ciba Pharmaceutical Products, Inc.

Sintrom

COMPOSITION: Double-scored tablets containing 4 mg. acenocoumarin.

INDICATIONS: Prophylaxis and therapy of thromboembolic disorders including coronary thrombosis, thrombophlebitis, arterial thrombotic occlusion, pulmonary embolism, selected cases of congestive heart failure, and cardiovascular surgery.

DOSAGE: Initial dose of 16 to 28 mg.; induction completed on second day with 8 to 16 mg.; usually, maintenance dose ranging from 2 to 10 mg.

PACKAGING: Bottles of 50 tablets.

SUPPLIER: Geigy Pharmaceuticals.

Syntocinon

COMPOSITION: Ampuls, 0.5 ml. containing 5 international units synthetic oxytocin (Syntocinon) and 1 ml. containing 10 international units.

INDICATIONS: Therapeutic induction of labor, stimulation of labor, management of labor at appearance of anterior shoulder, prevention and treatment of postpartum hemorrhage, postpartum atony; prepared by synthesis and does not contain amino acids characteristic of vasopressin, therefore lacking cardiovascular effects.

SIDE EFFECTS AND CONTRAINDICATIONS: Cephalopelvic disproportion; malpresentation of fetus; factors predisposing to uterine rupture, or to thromboplastin or amniotic fluid embolism; hypertonic patterns of uterine contractions; and inability of physician to be in attendance.

DOSAGE: For induction of labor, 10 I.U. dissolved in 1,000 ml. 5% dextrose, started intravenously at 0.5 ml. per minute; for management of labor at appearance of anterior shoulder, 2 I.U. intravenously.

PACKAGING: Boxes of 12 and 100.

SUPPLIER: Sandoz Pharmaceuticals.

Tussionex

COMPOSITION: Tablets containing 5 mg. dihydrocodeinone as resin complex and 10 mg. phenyltoloxamine as resin complex; liquid containing in each 5 ml. 5 mg. dihydrocodeinone as resin complex and 10 mg. phenyltoloxamine as resin complex (narcotic).

INDICATIONS: Antitussive, suppressing cough for 8 to 12 hours without abolishing natural protection of cough mechanism.

SIDE EFFECTS AND CONTRAINDICATIONS: None noted.

DOSAGE: 5 mg. (one tablet or 5 ml. liquid) every 8 to 12 hours.

PACKAGING: Tablets, bottles of 100; liquid, bottles of 16 ounces.

SUPPLIER: R. J. Strasenburgh Co.

V-Cillin K

COMPOSITION: Tablet containing 125 mg. (200,000 units) or 250 mg. (400,000 units) penicillin V (V-Cillin K) potassium.

INDICATIONS: Infections due to penicillin-susceptible pathogens.

DOSAGE: 125 to 250 mg. three times daily.

PACKAGING: 125 mg. tablets in bottles of 50; 250 mg. tablets in bottles of 24.

SUPPLIER: Eli Lilly and Company.

Zactirin

COMPOSITION: Tablets containing 75 mg. ethoheptazine citrate and 0.3 Gm. acetylsalicylic acid.

INDICATIONS: Relief of moderate to moderately severe pain, especially in ambulatory patients.

SIDE EFFECTS AND CONTRAINDICATIONS: Infrequent and minor, include transient nausea, epigastric distress and dizziness.

DOSAGE: Two tablets 3 or 4 time daily; total daily dosage should not exceed 8 tablets.

PACKAGING: Bottles of 48.

SUPPLIER: Wyeth.

SELECTED PHARMACEUTICAL ABSTRACTS

and summaries of other articles interesting to hospital pharmacists

edited by CLIFTON J. LATIOLAIS *and* LEO F. GODLEY

VITAMIN D STABILITY

Stability of Vitamin D in Pharmaceutical Preparations as Well as in Nutrient Salt Mixtures, Gebauer, H., Ackermann, H., and Tschapke, H., Die Pharmazie 12:265 (May) 1957.

Forty-eight Vitamin D preparations were assayed for Vitamin D stability according to a recent chemical method and a biological 'seven day prophylactical' test on albino rats; both methods show results which agree. The preparations (from USA, Germany, Switzerland, Holland, USSR) were stored at room temperature up to nine years.

A list of the assayed Vitamin D preparations was given including the declared concentration of Vitamin D activity and the assay results. Generally, there was found a high Vitamin D content even after three years storage except in nutrient salt mixtures. The authors suggested that the date of manufacturing and expiration be included on the preparation.

OTMAR NETZER

IODINE AND IODIDES, QUANTITATIVE ASSAY

A Contribution to the Control of the Purity of Iodine and Iodides, Berka, A. and Zyka, J. Ceskoslov. Farm. 6:110 (Feb.) 1957.

N-bromosuccinimide is an oxidizing agent which has been studied lately with the idea of using it in oxidimetric titrations. In this work the results obtained were applied to the quantitative control of the purity of iodine and iodides.

In the case of iodine the presence of iodine chloride does not interfere. The determination of iodides was not interfered by the presence of bromides and chlorides.

The titration is carried out in solutions which are sufficiently acidified with hydrochloric acid, iodine chloride is the final product of the oxidation. The point of equivalence is controlled by a potentiometer. The determination can be done in microscale and is suitable for the titration of iodides when a large excess of bromides and chlorides prevails. The proposed method was applied to the determination of iodides in ointments and in Lugol's solution. The determination in iodine tincture is interfered with by the presence of ethanol.

Attention is drawn to the fact that N-bromosuccinimide is suitable for the titration of arsenites and hydrazine and some of their derivatives. It was applied to determine arsenic in Fowler's solution and for the control of isonicotinic acid hydrazide. It is possible to titrate either potentiometrically (in microquantities) or visually using methyl red as indicator. (Institute of Analytical Chemistry, Charles University, Prague)

AUTHOR'S SUMMARY

PYROGENS, A NEW TEST FOR

Experimental Studies on the Sensitivity of Guinea-Pigs to the Pyrogenic Factor. II., Sterba, O. and Jozova, O., Ceskoslov. Farm., 6:358 (July) 1957.

Results of tests are described for sensitivity of guinea-pigs to pyrogenic substances (intraperitoneal application) in comparison with intravenous application in rabbits in connection with investigations of rubber and metal transfusion material including its preliminary preparation, physiological saline, 5% solution of glucose, 20% solution of human albumin, and conservation solutions of blood ACD and ACDRA.

In rubber and metal transfusion material were always carried out 9 comparative applications; conforming results were obtained in eight cases out of nine. The response of the experimental animals to physiological saline was in conformity in 15 experiments out of 17.

Absolutely conforming results were obtained in experiments after application of 5% glucose solution (nine comparative experiments) and 20% solution of human albumin (five comparative experiments), likewise conservation solutions of blood ACD and ACDRA (12 comparative experiments).

The obtained results show that it is possible to carry out biological estimations of pyrogenic substances on guinea-pigs. (Institute of Hematology and Blood Transfusion, Prague.)

AUTHOR'S SUMMARY

ASSAY OF PHARMACEUTICALS IN NON-AQUEOUS SOLUTIONS

Volumetric Analysis of Pharmaceutically Employed Weak Acids and Bases in Non-Aqueous Solutions, Keller, W. and Weiss, F., Die Pharmazie 12:462 (Aug.) 1957.

Satisfactory results were obtained from the volumetric analysis of alkaloids (ephedrine, ephedrine hydrochloride), isonicotinic acid hydrazide, and some antihistamines, dissolved in non-aqueous acetic acid and titrated with perchloric acid, using crystal violet, scarlet red, malachite green, or alpha-naphthobenzeine as the indicator, in comparison to volumetric analysis in an aqueous solvent.

Because of a more complete reaction and no interference from the hydrolysis of the salt resulting from the titration, a sharper endpoint was obtained with the non-aqueous solvents than with the aqueous ones.

However, there were unsatisfactory results of the analysis of sulfonamides in acetic acid. Furthermore, volumetric analyses of sulfonamides and barbiturates were done in dimethylformamide or pyridine, the non-aqueous solvents, titrated with N/10 solutions of sodium or lithium methylate, thymol blue as indicator with good results.

OTMAR NETZER

APPARATUS FOR BREAKING AMPULS

Transferring Easily Oxidized Powders, Lewis, F. A., Chem. and Ind. 43:1415 (Oct. 26) 1957.

A procedure for breaking ampuls of easily oxidized powders has been devised. The method involves use of a vacuum tube with sealed in electrical leads. Breaking of an ampul contained in the vacuum tube is achieved by passing an electrical current through a wire wrapped around one end of the ampul. Advantages of the system are production of a large aperture, which facilitates transfer of ampul contents, and a minimization of glass fragmentation.

JOHN D. LUCASSE

VISCOSITY OF PHARMACEUTICAL SUSPENSIONS

Studies on the Pharmaceutical Suspension. III. On the Consistency. (1)., Awada, E. and Ueda, S., J. Pharm. Soc. Japan 77:710 (July) 1957.

Measurement of viscosity was carried out in a small and narrow range of the rate of shear on aqueous solution of sodium carboxymethylcellulose added with granules of procaine penicillin G, chloramphenicol, chloramphenicol palmitate, and talc, whose particle size distribution is known. They all showed a typical structural viscosity and the three, with the exception of talc, showed dependence on shear rate. There was a linear relationship between the logarithms of viscosity, nap, and rate of shear. Viscosity increases with increasing amount of the granules added but the absolute

value varies with the kind of the granule, though independent of the rate of shear. With the increasing amount of the granules, dependence of consistency on shear rate increases and structural viscosity becomes marked. This is assumed to be due to the formation of a floccule with the exception of talc.

AUTHOR'S SUMMARY

VISCOSITY OF PHARMACEUTICAL SUSPENSIONS

Studies on the Pharmaceutical Suspension. IV. On the Consistency. (2)., Awada, E. and Ueda, S., J. Pharm. Soc. Japan 77:716 (July) 1957.

Measurement of viscosity was carried out in a large and wide range of rate of shear on a suspension of five kinds of granules, including the four mentioned in the preceding paper and barium sulfate. All were found to be a Bingham body and showed a simple plastic flow as long as the amount of the granules added was small but exhibited hysteresis loop in the viscosity curve as the amount of granules increased, and the thixotropic coefficient, M, increased with the increase of yield value and plastic viscosity. In the present series of experiments, barium sulfate alone showed exceptional characteristics and both the yield value and plastic viscosity tended to decrease when the amount added was small.

AUTHOR'S SUMMARY

VISCOSITY OF PHARMACEUTICAL SUSPENSIONS

Studies on the Pharmaceutical Suspension. V. On the Spinnability. (1), Awada, E., J. Pharm. Soc. Japan 77:722 (July) 1957.

Measurements of viscosity were carried out on the same samples as those described in the preceding paper. In suspension of substances like talc, which does not have a strong thixotropic character, nap increases with the increasing amount of the granules added and spinnability, which is a lower-limit type, also increases. A transition point, at which the spinnability changes to the upper-limit type, is observed when nap becomes too large. When the amount of the granules added increases further, nap also continues to increase but spinnability decreases while still in the upper-limit type and finally disappears altogether. In a suspension with strong thixotropic character, nap increases with increasing addition of the granules at first and spinnability, which is a lower-limit type, also increases. With further increase in the amount added, the length of spinnability becomes definite, irrespective of the velocity of drawing and in spite of increasing nap. This is probably due to the marked appearance of thixotropic character with the increased addition to granules. Further increase in the amount results in the decrease of spinnability, irrespective of the velocity of drawing.

AUTHOR'S SUMMARY

INJECTIONS, EFFECT OF COPPER ON

The Content of Copper in Galenicals. V. The Aggressiveness of Injections Towards Copper, Schou, Svend Aage, Dansk Tidsskr. Farm. 31:157 (Aug.) 1957.

Sixty-four injections, which are included in the *Danish Pharmacopoeia*, were investigated to ascertain whether they attack copper. Preparations which dissolved less than 100 microgram copper per ml. after a reaction period of four weeks (200 ml. solution, 6.6 cm^2 copper surface) were designated mildly aggressive. Preparations which dissolved more than 100 microgram per ml. were designated strongly aggressive.

The least aggressive injection was, surprisingly, ascorbic acid, which had only dissolved 1 microgram per ml. in four weeks, whilst the most aggressive was pyridoxine, which had dissolved 4200 microgram copper in 1 ml. solution.

It has not been possible to draw up general rules for the degree to which copper is attacked by the different preparations. Half of the preparations tested were slightly aggressive and half strongly aggressive.

The relation of solutions of adrenaline and noradrenaline to definite amounts of copper ion (0.02-50 p.p.m.) was investigated. The solutions, which contained the amount of pyrosulphite prescribed in the *Ph. Dan.*, i.e. 0.05 percent, remained colorless as long as they contained sulphite. It was shown that just as sulphite inhibits the oxidation of adrenaline and noradrenaline, so these two compounds inhibit the oxidation of sulphite. It would appear that adrenaline and noradrenaline are first oxidized when all the sulphite is oxidized. Copper ions rapidly catalyse the oxidation of sulphite and then catalyse the oxidation of adrenaline or noradrenaline.

Amounts of copper of the order of 0.5-10 p.p.m. partially inhibit the oxidation of sulphite in solutions containing only pyrosulphite at the same pH as the injections of adrenaline or noradrenaline. It may be noted that on reaching a concentration of copper of 20 p.p.m., a catalytic effect on the oxidation begins to occur.

Catalytic oxidation by copper causes decomposition of medicaments containing this substance. As even traces of copper are significant, it is important that injections should not come into contact with copper or copper alloys (syringes, ampul-filling devices). Only copper-free water should be employed for substances which are easily oxidized e.g. adrenaline and noradrenaline. As a result of these experiments the *Danish Pharmacopoeia* now prescribes re-distilled water for solutions of adrenaline and noradrenaline.

AUTHOR'S SUMMARY

STERILIZATION OF DRUG AMPULS

Sterilization of Drug Ampuls, Queries and Minor Notes, J. Am. Med. Assoc. 165:2032 (Dec. 14) 1957.

A question was raised as to the advisability of sterilizing drug ampuls used in spinal anesthesia by autoclaving, repeatedly if necessary.

Carter and Associates (*Anesthesiology 15*:480, 1954) conclude that Novocain and Pontocaine can be sterilized up to five times. Pontocaine "Niphanoid" may lose its snow-like appearance after autoclaving and adhere to the sides of the ampul and thus reduce the solubility but the potency is not affected.

A second autoclaving of hyaluronidase and epinephrine may reduce the effectiveness of these drugs. Hyaluronidase and the sympathomimetics, such as epinephrine and Neo-Synephrine are much more heat-labile than local anesthetics.

Dextrose solutions may become discolored after more than one autoclaving.

It is emphasized that these drugs should not be re-autoclaved whenever it can be avoided.

CLIFTON J. LATIOLAIS

ASSAY OF PYRIDOXINE

Photometrical Determination of Pyridoxine in Pharmaceutical Preparations, Hrdy, O., and Urganova, L., Ceskoslov. Farm. 6:510 (Sept.) 1957.

The described method for determining pyridoxine in drugs is based on the reaction of pyridoxine with diethyl-p-phenylenediamine in the presence of oxidizing compounds. The resulting blue indophenol dye must be quickly extracted with benzene as it is very unstable in aqueous solution. The dye is stable in benzene solution and has the absorption maximum at 605 mu.

The determination is carried out by adding phospate buffer (pH 7), 1 ml. 0.1% solution of diethyl-p-phenylenediamine sulfate, and 10 ml. benzene to solution containing 10-200 ug pyridoxine. After adding 1 ml. 1% solution of potassium ferricyanide the resulting dye is immediately extracted with benzene. The determination is not interfered by presence of other vitamins of the B complex (B_1, B_2, B_6, Bc, PP, and B_{12}), nor of other compounds which combine with pyridoxine (e.g. biotin, methionine, choline, betaine), with the exception of ascorbic acid, salicylic acid, and phenol. Ascorbic acid interferes by reducing potassium ferricyanide and the added amount must be, therefore, proportionally increased. Salicylic acid gives a green dye sparingly soluble in benzene; it can be removed by extraction from the acidified solution prior to carrying out the reaction. Phenol gives a violet color (absorption maximum is at 580 mu). Its interfering influence can be abolished by subtracting the residue extinction from the found extinction after shaking the benzene solution of the dye with 5% boric acid; the colour belonging to pyridoxine is thus removed, while that of phenol is not changed. At pH 7 the dye is formed from phenol only slowly and thus there is extracted with benzene only a very small amount of the interfering colour. This enables to carry out a reliable determination of pyridoxine even in the presence of several times as great excess of phenol. (State Institute for the Control of Drugs, Prague.)

AUTHOR'S SUMMARY

FATTY AMINO ACID SURFACTANTS

A New Family of Amphoteric Surfactants: Fatty Amino Acid Derivatives, Anderson, D. L. and Freeman, A. J., J. Soc. Cosmet. Chem. 8:277 (Sept.) 1957.

A new family of surface active agents, the fatty amino acid derivatives, has recently been developed. These compounds occur in two classes, N-alkyl-beta-aminoproprionates (monoadducts) and N-alkyl-beta-imi-nodiproprionates (diadducts). The alkyl groupings are generally lauric, coco, or tallow fatty based chains. A neutralizing base of either sodium or triethanolamine is also present.

The electrochemical properties of the fatty amino acid derivatives render them amphoteric and therefore polyfunctional surfactants. They have a fatty amine salt activity in an acid system, a carboxylic acid salt activity in an alkaline system, and an inner salt (zwitterion) or nonionic activity in a neutral system.

The fatty amino acid derivatives have several characteristics of value in cosmetic formulations. Their amphoteric nature renders them compatible with nonionic, cationic, and anionic compounds. In emulsification where multicomponent surfactant systems are desired this property takes on added significance. Many exhibit high foaming properties which are desirable in shampoo formulations. Others have a high degree of substantivity or affinity for the skin and hair imparting softness and manageability to these tissues. The hydrotropic properties of certain of the diadducts makes them effective solubilizing agents for some organic (the chlorinated germicides are an example) and inorganic chemicals.

The fatty amino acid derivatives are available under the trade name of Deriphats from General Mills, Inc., Chemical Division, Kankakee, Illinois.

JOHN D. LUCASSE

MEASURING PERMEABILITY OF PROTECTIVE OINTMENTS

Investigation and Development of Protective Ointments I. Development of a Method for Measuring Permeation of Mechanical Barriers, Lueck, L. M., Wurster, D. E., Higuchi, T., Lemberger, A. P. and Busse, L. W., J. Am. Pharm. Assoc. (Sci. Ed.), 46:694 (Nov.) 1957.

The purpose of this study was to develop an apparatus and technique for measuring diffusion of chemical agents through a protective barrier as the first step in elucidating the manner in which protective ointments behave toward diffusing substances.

An apparatus is described which utilizes a thin supported membrane of the barrier ointment to separate two glass chambers, one containing a solution of the penetrating agent and the other containing pure solvent. The rate of diffusion of the penetrating agent through the barrier is determined by assaying aliquots of liquid from each side of the membrane after definite intervals of time.

Jelene and white petrolatum were used as barrier materials while aniline, nitrobenzene and isovaleric acid served as penetrants. Plotting the experimentally obtained data according to an equation derived from theoretical considerations it was possible to calculate a permeability constant, K, for each of the penetrants which serves as a semiquantitative indication of the rate at which a penetrant material passes through a given semisolid barrier.

WARREN MCCONNELL

PERMEABILITY OF PROTECTIVE OINTMENTS

Investigation and Development of Protective Ointments II. Influence of Partition Coefficient and Thickness, Lueck, L. M., Wurster, D. E., Higuchi, T., Finger, K. F., Lemberger, A.P., and Busse, L. W., J. Am. Pharm. Assoc. (Sci. Ed.) 46:698 (Nov.) 1957.

Using apparatus described in a previous paper, this study dealt with an evaluation of the effect on protective capacity of thickness of the barrier film, nature of the barrier material, and physical state of the penetrant in contact with the barrier surface, that is, whether in vapor or liquid phase.

Nitrobenzene was used as the penetrating agent in all experiments. Barrier materials were white petrolatum, Jelene, Kel F-150, combinations of cerese yellow wax in heavy liquid petrolatum and polyethylene glycol 400 monostearate. Solvents for the nitrobenzene were N-amyl sebacate, heavy liquid petrolatum, silicone DC 200 fluid, 1000 c.p.s., and various concentrations of ethanol in water.

Permeability constants, K, for the penetration of barrier materials by vapor and liquid phase penetration were determined by graphic solution of an equation (derived in a previous study) using experimentally determined data.

Results showed that the permeability constant varies directly with the distribution coefficient and that therefore the optimum base to be selected for a protective ointment is one in which the penetrating agent is poorly soluble.

The authors conclude that the experimental procedures outlined are valid for determining permeability of protective films to both liquid and vaporous penetrants.

WARREN MCCONNELL

SORBITOL SOLUTION AS STABILIZING VEHICLE

Aqueous Oral Preparations Containing Ascorbic Acid, Vitamin B_{12}, and Ferrous Gluconate, Gerber, C. F., Hetzel, C. P., Klioze, O., and Leyden, A. F., J. Am. Pharm. Assoc., (Sci. Ed.) 46:635 (Nov.) 1957.

Ascorbic acid and vitamin B_{12} are incompatible with each other and with iron salts in aqueous solution. An empirical study was made to determine the effect of a change of vehicle upon stability of combinations of these drugs. Formulations studied included a multivitamin solution, a hematinic solution and a liquid tonic. Solvents studied were composed essentially of water, 70% sorbitol solution, and/or glycerin.

Assays for ascorbic acid and vitamin B_{12} were performed on samples stored at 25° and 37° after 13, 26, and 52 week storage intervals. Preparations made with solvent containing 70% sorbitol exhibited least deterioration in spite of the fact that they contained a greater proportion of water than some solvents prepared with glycerin. The authors conclude that this may be attributed either to the greater water-bonding ability of sorbitol or to complex formulation between the vitamins and the polyol, or both.

WARREN MCCONNELL

VITAMIN B_{12} STABILITY

The Effect of Various Sugars and Polyols on the Stability of Vitamin B_{12}, Barr, Martin, Kohn, S. R., Tice, L. F., J. Am. Pharm. Assoc. (Sci. Ed.), 46:650 (Nov.) 1957.

Vitamin B_{12} is reportedly stable in vehicles containing sorbitol or glycerin but unstable in vehicles containing sucrose or dextrose. This study was performed for the purpose of comparing the stability under controlled conditions of this vitamin in vehicles containing each of these compounds.

Sterile samples containing 30 mcg. per ml. of vitamin B_{12} in 50% solutions of sorbitol, glycerin, dextrose, and sucrose were filled aseptically into 10-ml. ampuls and sealed. Samples were assayed spectrophotometrically at specified intervals of time after storage at 25°, 45°, and 100°. Results showed that stability of vitamin B_{12} is poorer under all conditions in the presence of dextrose and sucrose. Stability in solutions containing sorbitol or glycerin was greater than in pure water in samples stored at 100°. No loss of vitamin B_{12} was noted in samples containing sorbitol, glycerin or pure water stored at 25° and 45° even after 140 days aging.

WARREN MCCONNELL

OINTMENT BASES, MELTING BEHAVIOR OF

A Dilatometric Study of Melting Behaviors of Some Fats, Waxes, and Related Substances of Pharmaceutical Importance I., Ravin, L. J. and Higuchi, T., J. Am. Pharm. Assoc., Sci., Ed. 46:732 (Dec.) 1957.

Dilatometry is a valuable tool for the determination of phase characteristics of waxy substances. It consists of measuring the specific volume of substance as the temperature is raised from about 28° C to slightly above the melting point of the substance. It has great reproducibility and sensibility, and thus can serve as a control for substances of this nature. It should prove to be of great value in detecting solid solutions in pastes, bases, and other semi-solid systems. It can also be useful in elucidating solid state structures of many complex systems.

The technique was described and dilatometric curves between 28° C and a few degrees beyond their melting points were given for the following substances: Polyethylene glycol 4000, PEG 6000, PEG 20,000, a mixture of PEG 4000 and PEG 6000, spermaceti, cetyl alcohol, a

mixture of spermaceti and cetyl alcohol, a mixture of spermaceti and PEG 4000, a mixture of cetyl alcohol and PEG 4000, and white wax.

Data showed that the polyethylene glycols possess similar crystal structures in their solid states, and that the components form nearly ideal solutions in both the solid and melted phases. These studies show also that polyethylene glycol ointment base contains a higher percentage of solids than does white petrolatum of the same consistency.

When two immiscible substances such as spermaceti and PEG 4000 are mixed, they melt independently of each other, and the mixture has little effect upon the melting points of the individual components.

When two miscible substances such as spermaceti and cetyl alcohol are mixed, the individual melting points cannot be detected, and their mixing has a pronounced effect upon the final melting point.

Sudden or shock cooling did not change the dilatometric curves of white petrolatum and polyethylene glycol. On the other hand oil of theobroma exhibited a marked difference between samples which were shock cooled and samples which were cooled slowly. The shock cooled samples showed an expansion between 16 to 20° C, and a contraction between 20 and 24° C. This may explain why suppositories which have been cooled suddenly may have unusually low melting points.

PAUL J. NIEBERGALL

CLEANSING CREAMS, MODE OF ACTION

Fundamental and Comparative Actions of Cleansing Creams, Latven, A. R., J. Soc. Cosmet. Chem. 8:300 (Sept.) 1957.

Research conducted to determine the mode of action of cleansing creams has revealed that these products exert their cleansing action chiefly through the removal of sebum and its accompanying foreign matter which has solidified as "plagues" over the sebaceous or pilosebaceous orifices (pores) of the skin.

Experimentally a cleansing cream or other cleansing agent was applied to the skin of subjects for a period of fifty minutes. Subsequently, the treated areas and adjacent untreated areas were examined for changes in sebum deposit. This examination was done using ultraviolet light which readily detects the fluorescent sebum.

Results showed that cleansing creams, although differing in degree, definitely aided in removal of sebum "plagues." Emulsifying agents, such as soaps, Tweens and Spans, and the organic solvents did not.

These two latter groups of agents also were shown to remove the skin's natural liquid film. The cleansing creams left this protective layer intact, further increasing their value in skin care.

JOHN D. LUCASSE

ASPIRIN ELIXIR

Aspirin Elixir, Schwarz, T. W., Shvemar, N. G. and Renaldi, R. G., J. Am. Pharm. Assoc., Pract. Pharm. Ed. 19:40 (Jan.) 1958.

A formula for an aspirin elixir was developed. When the product was stored in a refrigerator at an average temperature of 6°C., only 6% of the aspirin hydrolyzed in 5 weeks. The authors present the following formula as one useful for extemporaneous compounding of an aspirin elixir to be used within a month. Although aspirin hydrolyzed less in propylene glycol than in polyethylene glycol 400, the latter was used in the vehicle because the authors found it difficult to mask the taste of the former. Calcium cyclamate (Sucaryl) produces less hydrolysis than the sodium salt.

Formula: Aspirin 2.5 Gm.; Sucaryl 3.5 Gm.; Soluble Orange 0.25 ml.; Alcohol 20.0 ml.; Purified Water 15.0 ml.; and Polyethylene Glycol[1] 400, to make 100.0 ml.

[1] May be replaced with propylene glycol.

DON E. FRANCKE

NEW SUPPOSITORY BASE

"Massupol"—A New Suppository Base, Paviour, Janet, Australasian J. Pharm. 38:1027 (Sept. 30) 1957

A comparative study was made of oil of theobroma and "Massupol" as suppository bases. "Massupol" consists essentially of glycerol esters, mainly of lauric acid with a small amount of gycerol monostearate added to improve its water absorbing properties. Unlike oil of theobroma, "Massupol" can be heated above its melting point without a change in its physical state. On cooling the base contracts slightly which eliminates the need of a mould lubricant in suppository compounding. Unlike oil of theobroma, "Massupol" has no unsaturated linkages. For this reason it is not affected by metallic ions or the danger of rancidity from long storage. ("Massupol" is available from Watts Winter Pty. Ltd., Sidney Australia)

A. J. GIBSON

STABILITY OF OXOCAMPHOR

Pharmaceutical Applications of Inclusion Compounds, I. Stabilization of d-trans-8-Oxocamphor by Formation of Thiourea Adduct., Mima, H., J. Pharm. Soc. Japan, 77:1196 (Nov.) 1957.

d-trans-8-Oxocamphor is used widely as a cardiotonic but its crystal is extremely unstable and is oxidized in the air, almost completely losing its pharmacological effect in about 24 hours. A methanolic solution of this substance and thiourea separates some needle crystals on being cooled and the newly formed substance is composed of 8-oxocamphor and thiourea in 1:3 molar ratio. From x-ray diffraction and infrared absorption spectrum, the crystal is a rhombohedral and the substance was proved to be the so-called inclusion compound by Schlenk and others. Such 8-oxocamphor included in thiourea is extremely stable and residual ratio after 8 months at room temperature was 97.5%, that after 6 months at 40° being 93%. Extraction of this adduct in a Soxhlet extractor with warm ether was found to give 100% of 8-oxocamphor and the residual thiourea formed the original rhombic crystals. When this adduct is dissolved in water, it dissociated into the original two components, the solution showing the chemical properties of 8-oxocamphor, as well as its toxicity and pharmacological effect. There was no difference in its effect as a medicinal from the corresponding 8-oxocamphor.

AUTHOR'S SUMMARY

NEW ISOTONIC SOLUTION VALUES

New Isotonic Solution Values, Hammarlund, E. R. and Pedersen-Bjergaard, K., J. Am. Pharm. Assoc., Pract. Pharm. Ed. 19:38 (Jan.) 1958.

The authors have recently experimentally determined new sodium chloride equivalents for a large number of drugs (to be published in the *J. Am. Pharm. Assoc. Sci. Ed.*). Using the sodium chloride equivalents for individual 1% solutions of each of the drugs, a table has been compiled showing the volume in ml. of water required to dissolve 0.3 Gm. of various drugs before adding isotonic diluting fluid in order to prepare 30 ml. of a solution isotonic with blood serum or tears and containing 1% of the specified drug. This table, composed of values for approximately 220 drugs, represents a revision of the values originally assigned by Sprowls and includes values for numerous additional drugs.

DON E. FRANCKE

RELIGION AND MEDICINE

Interrelationship of Religion and Medicine, Blake, E. C., Silver, A. H. and Wilders, J. G., N. Y. State J. Med. 57:1651 (May 1) 1957.

Three somewhat different, but yet converging views upon the relationship between religion and medicine are presented by three clergymen. One view set forth states that the physician should certainly realize that the health of an individual is concerned with the *whole* man; for man has more than just a body, he possesses a soul or spirit. It is quite futile for the physician to be interested merely in patching up a worn out and oft times abused physical body and to think that he can thereby produce health. Health is subordinate to the prime purpose in life and never should be the ultimate end.

A second view traces the thread of medicine backward into time and finds it interwoven with the fabrics of religion. Often, in ancient times, it occurs that the religious leader and physician were one and the same. Perhaps this interfusion grew from the basic religious concept and conviction that the soul and body are both God's handiwork and must be carefully tended. These substances, the body—tangible, and the soul—intangible, constantly interact in an intricate and involved manner. Thus, the health or infirmity of one greatly affects the soundness of the other. A great number of psychologists have pointed out that persons

fall emotionally ill because they have lost that intangible something which religious beliefs offer. Nowadays counseling agencies have been established by a number of churches and synagogues to help those with serious emotional problems. After talking with the person, the minister will often direct the worried individual to a professional psychiatrist. The health and well being of society might be said to be based upon principles and disciplines which are religious in their inspiration.

The final facet of this interrelationship was that of the interworking of the physician and the clergyman. A religious patient has an unmistakable right to expect the physician to understand that his belief plays a vital part in his life. It has to do with a most basic concern —the meaning of life. It is often important that the patient receive words of consultation and guidance from a clergyman. Religious counseling prepares the patient, calms his apprehensions, and gives courage and confidence to him.

By being sympathetic to the religious as well as the medical needs of his patients, the physician is fulfilling his responsibility to provide, as far as he is able, for the total needs of those who come to him for care.

ROBERT W. MAHONEY

PHARMACY IN THE SOVIET UNION

Pharmacy in the Soviet Union, Atkinson, R. G., Pharm. J., 125: (4th series) 427-430 (Nov. 30) 1957.

The author reports on the scope and activities of Russian pharmacy based on a recent visit to the Soviet Union.

At present, a five-year course of study is required for pharmacy practitioners. Generally, students matriculate in pharmacy schools at the age of 17 after having passed competitive examinations in chemistry, physics, Russian language and literature, philosophy and a foreign language. All full-time pharmacy students are paid a stipend with extra money awarded to superior students. The curriculum is similar in many respects to that offered in pharmacy schools in this country, except that the Russian student receives a Marxian indoctrination. The five-year academic program may be interrupted after the third year of study, during which time the student can work two or three years in a drug store, and then return to pharmacy school for the remaining two years. Under certain conditions it is now possible to meet the requirements of pharmacy education through correspondence courses. Graduate work in pharmacy is available to students who are paid while pursuing three years of advanced work. All military pharmacists are accorded officer status. There are currently about 8,000 students enrolled in pharmacy schools throughout the U.S.S.R. The five-year pharmacy syllabus is sponsored jointly by the Minister of Health and the Minister of Higher Education. Pharmacists belong to the Trade Union of Medical Workers.

All retail pharmacies are nationalized. While no women were allowed to work in drug stores prior to the Revolution, today about 90% of the Russian pharmacists are women. Drug prices are fixed by the government, and a nominal fee (about 2 roubles) is paid by patients for each prescription with the exception of insulin and other specified medications which are free.

A national pharmaceutical journal, *Aptechnoe Delo* (Pharmaceutical Affairs) is published every two months, and contains pharmacy reports, book reviews, research papers and historical articles. A revision of the 8th edition (1952) of the official *State Pharmacopoeia of the U.S.S.R.* is nearing completion.

All hospitals with 100 beds or more have pharmacy departments, while those institutions having fewer than 100 beds receive service from local pharmacies. There are no separate hospital formularies, nor do pharmacists give pharmaceutical instruction in teaching hospitals.

At present, the U.S.S.R. imports comparatively few drugs and is rapidly becoming self-sufficient in the manufacture of medicinals. The Soviet Minister of Health admits frankly that "the medical supplies industry, however, does not yet fully meet the needs of the health services as regards drugs, medical instruments, and equipment, especially the most up-to-date preparations and apparatus." In the last 15 years, production of chemicals has tripled.

Pharmaceutical research is being carried out in various institutions throughout the U.S.S.R. A great deal of research is concentrated on medicinal plants. Examples of recent pharmaceutical research papers are as follows: 1. Manufacture of sintomycin free from bitterness. 2. Phytochemical investigation of the flowers of *Helichrysum arenarium*. 3. Antibacterial properties of oak leaves. 4. Application of photocolorimetry in analyzing medicinal mixtures. 5. Polyethylene oxide as a binding agent in the production of tablets. 6. The use of tungsten-phosphoric acid for the quantitative determination of sulfanilamide preparations.

Pharmacists receive approximately 1,200 roubles per month as compared with a waiter (600-900 roubles), a school teacher (1050-2300), a professor (4500-5000), a bus driver (900-1000). A pharmacist receives one month's vacation a year and is entitled to an old-age pension of 40-50% of earnings after 25-30 years of work.

ALEX BERMAN

CURRENT LITERATURE

. . . also calling your attention to the following articles appearing in recent hospital and pharmaceutical journals

. . . . . .

ADMINISTRATION

—Packaging

Raine, G.: Aluminum-Foil Overseals, *Public Pharmacist* (Great Britain) 15:26 (Jan.) 1958.

—Stock Control

Teplitsky, Benjamin: What To Look For in the Drug Cabinet, *Modern Hosp.* 90:88 (Jan.) 1958.

FLOOR PLANS AND PLANNING

Anon.: Hospital Pharmacy Planning, 4. Furniture and Fittings, *Public Pharmacist* (Great Britain) 15:31 (Jan.) 1958.

MANUFACTURING

—Equipment

Grainger, H. S.: Functional Test on a New Device for Blending Pharmaceutical Mixtures, *Public Pharmacist* (Great Britain) 15:25 (Jan.) 1958.

PARENTERAL SOLUTIONS

Grainger, H. S. and Smith, Margaret D.: Temperature Variation in Ovens Used For Sterilising Pharmaceutical Products, *Public Pharmacist* (Great Britain) 15:39 (Jan.) 1958.

PHARMACOLOGY AND THERAPEUTICS

Domino, E. F.: Pharmacology of the Central Nervous System, *Progress in Neurol. and Psychiat.* 12:92 (Dec.) 1957.

Friend, Dale G.: Current Concepts in Therapy, Analgesic Drugs VII. Narcotics I, *New England J. Med.* 257:985 (Nov. 14) 1957.

Friend, Dale G.: Current Concepts in Therapy, Analgesic Drugs VIII. Narcotics II, *New England J. Med.* 257:1182 (Dec. 12) 1957.

Himmich, H. E.: Psychopharmacologic Drugs, *Science* 127:59 (Jan. 10) 1958.

Anon: A.M.A. Hears Reports on Hospital Infections, *Modern Hosp.* 90:49 (Jan.) 1958.

Anon.: Acute Convulsive Disorders in Children, *Modern Hosp.* 89:98 (Dec.) 1957.

PHARMACY AND THERAPEUTICS COMMITTEE

—Dangerous Drugs

Huffman, Edna K.: Medical Records—Stop Orders On Dangerous Drugs, *Hosp. Management* 85:72 (Jan.) 1958.

—Investigational Drugs

Archambault, G. F.: Guest Editorial—Investigational Drugs, *Hospitals* 32:35 (Jan. 1) 1958.

Kerlikowske, A. C. and Francke, D. E.: Responsibilities of the Hospital Staff, *Hospitals* 32:45 (Jan. 1) 1958.

Sessoms, S. M.: Guiding Principles in Medical Research Involving Humans, *Hospital* 32:44 (Jan. 1) 1958.

POISON CONTROL

Cann, Howard M.: National Clearinghouse for Poison Control Centers, *Hospitals* 32:42 (Jan. 16) 1958.

Wheatley, George M.: Poison Control Centers, *Hospitals* 32:38 (Jan. 16) 1958.

SMALL HOSPITALS

Berman, Alex: Pharmacy Service in Smaller Hospitals (Part II), *Am. Profess. Pharm.* 24:50 (Jan.) 1958.

Moravec, Daniel F.: Pharmacy Service in Smaller Hospitals—Part III, What Can Be Done To Improve It? *Hosp. Management* 85:120 (Jan.) 1958.

Anon: Drug Prices, *Modern Hosp.* 89:47 (Dec.) 1957.

SURVEYS

(see also Small Hospitals)

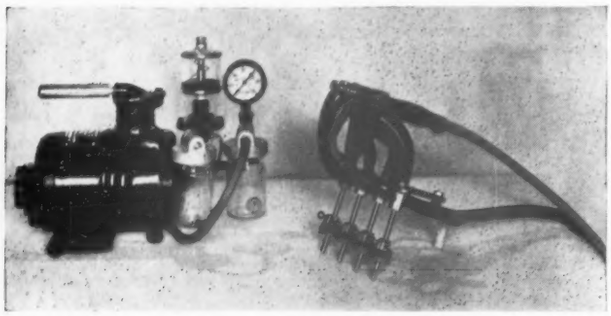
Block, Louis: Prototype Study: 75 Bed Proprietary Hospital, *Modern Hosp.* 90:80 (Jan.) 1958.

Notes + Suggestions

edited by CLIFTON J. LATIOLAIS

PORTABLE VACUUM FILLER

The Horix Model TV Portable Vacuum Filler* is useful for filling light or heavy liquids of all kinds. The standard outfit consists of a self-contained motor driven vacuum unit, filling head with adjustable filling valves, two-gallon overflow jar and vent, vacuum and liquid hoses. The pump is equipped with an automatic oiler, which operates only while the pump



is running. The filling head is made of aluminum and carefully balanced so that it is easy to insert the filling valves in the bottles. The filling valves can be easily adjusted or replaced to suit various sized bottles. Standard filling valves are stocked in ¼", 5/16", and ⅜" sizes or special sizes are available in stainless steel.

STORAGE OF N/10 NAOH

Solutions of sodium hydroxide stored in glass bottles cause flaking of the glass and the strength of the solution itself rises appreciably after a few weeks.

Easterbrook and Cameron report in the August 24, 1957 issue of *Chemistry and Industry* (page 1155) that the strength of 0.1N sodium hydroxide solution stored in a soda glass bottle for 15 months increased by 1.4 percent. Under similar conditions, NaOH (0.1N) solution stored in a polyethylene bottle was not affected.

Sodium hydroxide solutions (0.1N) stored in polyethylene bottles have greater stability and reliability as to strength than similar solutions stored in soda glass bottles.

*Horix Manufacturing Co., 2609 Chartiers Ave., Pittsburg 4, Pa.

ELIXIRS OF BARBITURATES

Improved formulas for phenobarbital and pentobarbital elixirs are reported by Barr and Tice in the September 1957 issue of the *Am. J. Pharm.*, page 332. These elixirs, according to the authors, are similar in *p*H, appearance and taste to Phenobarbital Elixir U.S.P. XV and Pentobarbital Elixir N.F. X. These formulations do not require filtration and remain clear at 25° C. and 4° C. In addition, ingredient costs are lower than the official formulas. The formulas suggested are:

Phenobarbital Elixir	
Phenobarbital	4.0 Gm.
Orange oil	0.25 ml.
Amaranth solution USP	10.0 ml.
Alcohol	200.0 ml.
Propylene glycol	100.0 ml.
Sorbitol solution, NF	600.0 ml.
Purified water, to make	1000.0 ml.

Dissolve the phenobarbital in the alcohol, add the propylene glycol, orange oil, sorbitol solution, and amaranth solution. Mix well, and add sufficient purified water to make 1000 ml. Mix well.

Pentobarbital Elixir	
Pentobarbital sodium	4.0 Gm.
Sweet Orange Peel Tincture	30.0 ml.
Alcohol	200.0 ml.
Propylene glycol	100.0 ml.
Sorbitol solution, NF	600.0 ml.
Diluted hydrochloric acid	6.0 ml.
Caramel	2.0 Gm.
Purified water, to make	1000.0 ml.

Dissolve the pentobarbital sodium in 60 ml. of water. Add the sorbitol solution, alcohol, propylene glycol, sweet orange peel tincture, and caramel. Mix well and add the diluted hydrochloric acid. Add sufficient water to make up to volume. Mix well.

SUPPOSITORY MOLDS

An illustrated booklet describing the different types of suppository moulds is available from Pharmetic Molds, P. O. Box 194, South Orange, New Jersey.

RARE CHEMICALS - SOURCES OF SUPPLY

The National Registry of Rare Chemicals provides a free service to inquirers by directing them to sources of supply for rare chemicals not readily available. Like a detective bureau, the Registry will cull its extensive files for information, check with specialists, refer to catalogs, chemical abstracts and books. Most of the inquiries are answered at once—the remainder are searched out until found.

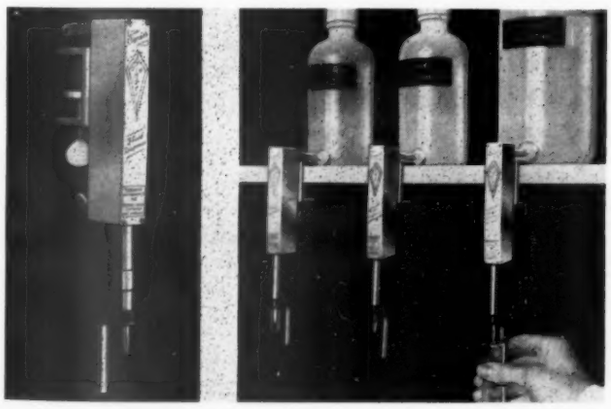
If you are trying to locate sources of supply of chemicals, perhaps the Registry can help you. Their address is: National Registry of Rare Chemicals, Armour Research Foundation, Technology Center, Chicago 16, Illinois.

PHARMACEUTICAL EQUIPMENT CATALOG

A new catalog file describing the complete line of Colton pharmaceutical and chemical machines and equipment is available on request from The Arthur Colton Company, 3400 East Lafayette, Detroit 7, Michigan. The file includes descriptions and photos on tablet presses, filling equipment including liquid fillers, tube fillers, triturate machines, hand capsule fillers, and other Colton machines.

FLUID DISPENSER

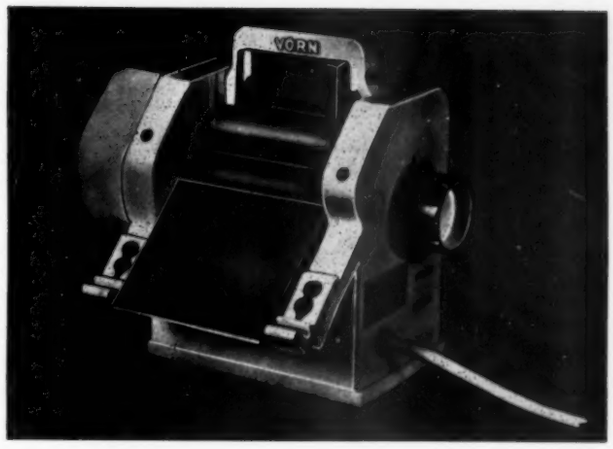
The L-9500-S Corinth Finger-Tip Fluid Dispenser* is designed for frequent dispensing of small amounts of fluids such as reagents, pharmaceuticals, corrosives, volatile solvents, etc. It can be drop-calibrated for quantitative delivery of milliliter amounts. It will deliver one pint or more per minute in full-opened



position. Recommended for use with bottom-tubulated aspirator bottles utilizing gravity feed or with siphon feed from standard containers and storage carboys.

It is constructed of stainless steel and anodized dichromate-sealed aluminum components. Dispenser complete with Pyrex brand nozzle, shield and Nalgon delivery tubing costs $17.50.

*Palo Laboratory Supplies, Inc., 81 Reade St., New York 7, N.Y.



OINTMENT MILL

The Hammonia Ointment Mill (Miniature Model)* is one of the smallest ointment mills on the market. Dimensions are 8″ x 5″ x 7″ and it weighs only 13½ pounds. It has an output of about 12 pounds of ointment per hour and mills small quantities with a minimum loss. It features easily adjustable fixed triple rolls of prophyry 3¼″ long x 1¼″ in diameter.

In addition to the Miniature, a regular model is available which has a 36 pound per hour capacity. Its dimensions are 17½″ x 10½″ x 11½″. Both the Miniature and regular models are designed for small volume manufacturing.

*The Burnet Company, East Midland Avenue, Paramus, N.J.

PARALDEHYDE ENEMA, B.P.C.

Paraldehyde	100.0 ml.
Sodium chloride	8.1 Gm.
Water, to make	1000.0 ml.

Dissolve the sodium chloride in the water and add the paraldehyde and mix.

*British Pharmaceutical Codex, 1954, page 975.

NAPHAZOLINE NASAL DROPS, B.P.C.*

Naphazoline nitrate	0.57 Gm.
Dilute acetic acid	1.04 ml.
Dextrose	50.0 Gm.
Chlorobutanol	4.57 Gm.
Water, to make	1000.0 ml.

Dissolve.

*British Pharmaceutical Codex, 1954 page 1082.

DEODORANT FOOT POWDER

Hexamethylenetetramine	3.0 Gm.
Talc	80.0 Gm.
Colloidal kaolin, absorbant	20.0 Gm.

The hexamethylenetetramine acts as a deodorizer by releasing minute quantities of formaldehyde in the presence of perspiration (*Drug and Cosmetic Industry 81*:109 (July) 1957.)

Consulting WITH BOWLES

GROVER C. BOWLES JR., *Baptist Memorial Hospital, Memphis, Tennessee*

► What facilities and personnel should be available before a hospital offers an internship in hospital pharmacy?

The Minimum Standard for Pharmacy Internship in Hospitals sets forth the specific qualifications for the hospital and the pharmacy service offering a pharmacy internship. The following is taken from the 1957 revision of the Standard:

"Qualifications of the Training Hospital"

"The hospital shall be a general hospital accredited by the Joint Commission on Accreditation of Hospitals and meeting in full the pharmacy elements of the accreditation schedule. In addition, the hospital must be approved for medical internship training by the Council on Medical Education in Hospitals of the American Medical Association. Pharmacy internships shall be conducted only in those hospitals in which the educational benefits to the intern are considered of paramount importance."

"Qualifications of Pharmacy Service"

"The pharmacy service shall comply with the requirements of the Minimum Standard for Pharmacies in Hospitals as approved by the Division of Hospital Pharmacy of the American Pharmaceutical Association and the American Society of Hospital Pharmacists. In addition to the pharmacist-in-charge, there shall be at least one full time registered pharmacist for each full time intern.

The pharmacy shall comply in full with all federal, state and local laws, codes, statutes, and regulations, including Food and Drug and Public Health Laws and Regulations and State Hospital Licensing Act and regulations for pharmacy service in hospitals.

The pharmacy shall provide the following minimum activities or divisions of pharmacy practice:

A. Administration
B. Inpatient and general dispensing
C. Outpatient dispensing
D. Bulk compounding and preparation of sterile products
E. Bulk compounding and prepackaging of non-sterile products."

► What is the approximate cost of the non-carbon duplicator paper and where may it be purchased?

Several years ago, the National Cash Register Company developed and marketed a non-carbon duplicating paper. It is available from the National Cash Register Company under the name, "NCR Paper—No Carbon Required." It is my understanding that the same or similar papers are available from firms specializing in business forms.

The cost of forms made from this type of paper is usually slightly higher, particularly when purchased in small quantities, than the typical form interlaced with carbon paper.

Contact the local branch of the National Cash Register Company and firms specializing in business forms for specific details about cost and types of forms available.

► What is a reasonable policy dealing with credit on medications returned from patients?

Policies dealing with refunds to patients for unused medication returned to the pharmacy vary from hospital to hospital. However, it seems reasonable to me to credit the patient's account with drugs returned to the pharmacy when the value amounts to one dollar or more. Of course, refunds should be allowed only when the medication may be positively identified and where no question exists as to possible contamination.

Where possible the pharmacist should limit the cause for refund by dispensing small quantities of expensive drugs and keeping the staff informed about the current cost of drugs. Certainly the patient has a just right to expect that his drug charges will be made in a fair and just manner.

► Should we buy or manufacture narcotic ampuls?

The production of ampuls is a time consuming task unless automatic or semiautomatic washing, filling, and sealing equipment is available. This equipment is designed for large scale production and is too costly for hospital use.

You may wish to consider the packaging of injectable narcotic solutions in multiple dose vials which can be accomplished economically and well by the hospital pharmacists. Should you prefer a single dose container consideration might be given to the use of rubber stoppered vials of 1 or 2 ml. capacity. Such vials are available for use with aluminum seals or the regular skirted rubber stopper. However, cleaning of large numbers of small vials may present some problems unless the proper equipment is available.

► Should all hospitals, regardless of size, have a Pharmacy and Therapeutics Committee?

Yes. The role of the Pharmacy and Therapeutics Committee in the promotion of rational drug therapy and, in turn, better patient care, is well established. This important role is in no way related to the size or bed capacity of the hospital.

DRUG EVALUATIONS

by the Council on Drugs of the American Medical Association

► THE FOLLOWING MONOGRAPHS and supplemental statements on drugs have been authorized by the Council on Drugs of the American Medical Association for publication and inclusion in *New and Nonofficial Drugs*. They are based upon the evaluation of available scientific data and reports of investigations. In order to make the material even more valuable, dosage forms and preparations of individual drugs have been added to the monographs. These dosage forms and preparations were not taken from material published in the *Journal of the American Medical Association* by the Council on Drugs; rather, they were obtained from such manufacturers' brochures, news releases, etc., which were available to us at the time of publication. An attempt has been made to make the list of dosage forms as complete as possible. However, no guarantee can be made that the list of preparations is complete and it is suggested that hospital pharmacists consult manufacturers' releases for additional dosage forms and preparations.

The issues of the *Journal of the American Medical Association* from which each monograph has been taken is noted under each monograph. Monographs in this issue of the JOURNAL include those published in the *Journal* to December 31, 1957.

Notice

New and Nonofficial Remedies 1957 is now available from your local bookstore and from the publishers, J. B. Lippincott Company, Philadelphia, Pa. This 1957 edition contains monographs of drugs evaluated by the Council on Drugs of the American Medical Association and published in the Journal of the A.M.A. to October 1956. The index listed below contains those drugs evaluated and published between October 1, 1956 and December 31, 1957.

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Infectious Hepatitis Current Status of Therapy of

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned. When such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. Kautz, M.D., *Secretary.*

Franklin M. Hanger, M.D., New York

Viral hepatitis varies in severity from a disturbance that is practically symptomless to a grave disorder marked by jaundice, prostration, and all the features of hepatic insufficiency. Treatment, therefore, cannot be uniform. There is abundant evidence, however, from studies in the armed forces and elsewhere, indicating that the average case is a self-limited affair and will run a satisfactory course irrespective of the details of clinical management. In recent years there has been a tendency to overtreat rather than undertreat this disease.

Studies of the natural course of hepatitis, acquired either through the oral or the parenteral route, indicate that there is an initial viremia with subsequent development of functional and cytological derangements of the hepatic parenchyma. The process usually leads to necrosis of the more severely affected cells. Adding to the primary disability is involvement of the cells lining the sinusoids, creating local disturbances of blood supply within the liver. Also, the supporting mesenchymal structures often show swelling and cellular infiltration, causing compression of channels such as cholangioles, lymphatics, and branches of the portal vein. Symptoms such as pain and abdominal discomfort are due largely to hepatic swelling and congestion of the splanchnic bed. Jaundice and digestive disturbances are attributable to derangements of the metabolic and excretory activities of the liver. The virus is not known to affect other organs of the body, but the fever, malaise, adenopathy, skin rashes, and arthralgias occurring early in the disease indicate a generalized toxic reaction to the offending agent and probably to the breakdown of hepatic tissue. Healing is usually complete after several months, with residual scars found only where massive necrosis and collapse of the lobular structures have occurred.

Treatment of the Average Case

The disease may be extremely difficult to recognize in the preicteric phase, unless enlargement or tenderness of the liver happens to be present or darkening of the urine is noted. In any event, the lack of leukocytosis warrants expectant, symptomatic treatment only, and uncritical administration of antibiotics is not justified. It is at this stage that the viability of affected liver cells is a prime concern, and the conservation of hepatic parenchyma can be most effectively attained by maintaining the patient at bed rest. No virucidal agent has yet been devised. Immune serum globulin (gamma globulin), which is a recommended prophylactic against virus A (1 H.), is of no therapeutic value. The use of adrenal steroids (glucocorticoids) in the average case of hepatitis is not indicated at this stage, despite the fact that these agents may ameliorate many of the disagreeable features of the disease. In addition to the risks of gastrointestinal bleeding, mental disturbances, and activation of latent infections induced by cortisone and its homologues, there is the theoretical hazard of disseminating the virus before sound immunity has developed. The severity of relapses sometimes observed after withdrawal of the drugs seems to bear out this point of view. At the present time, at least, it is deemed more prudent to withhold adrenal

From the Department of Medicine, Columbia University College of Physicians and Surgeons, and the Presbyterian Hospital.

steroid therapy for special situations which will be discussed later.

Anorexia is often a prominent initial symptom, with the patient showing a preference for fruit juices, ginger ale, sour candies, gruels, gelatin, and sherbets rather than for meats or fatty foods. Little is to be gained by forcing a high-protein or high-caloric diet during the acute phase of hepatitis, but adequate hydration is an important consideration. If there is vomiting or unwillingness to drink liquids, infusions of 1,000 cc. of 5% dextrose in water should be administered by slow drip once or twice during 24 hours. Epigastric burning, hiccough, and vomiting are usually relieved by a sodium-free alkali preparation and antihistamines, such as diphenhydramine (Benadryl) hydrochloride, 50 mg. before meals. Short-acting barbiturates and codeine or meperidine (Demerol) hydrochloride are not contraindicated for sleeplessness and pain, but they may mask symptoms and become increasingly hazardous with the fall of functional hepatic reserve. Bowel regulation is maintained by saline cathartics in the mornings before breakfast and by cleansing enemas.

With the appearance of jaundice there is usually a subsidence of fever and malaise and a return of appetite. It is then possible to give a simple, well-balanced diet of 2,000 to 3,000 calories, including cream and butter, tender fresh meats (except pork and oily fish), cooked fruits, puréed vegetables rich in carbohydrates, and simple desserts. It is regrettable that so many physicians still entertain the impression that fats are injurious in viral hepatitis. Observations on animals indicate that fats augment the toxicity for the liver of certain agents such as carbon tetrachloride, but there is no contraindication for eggs and fresh dairy products in the presence of uncomplicated infection. Indeed, these foodstuffs, when well tolerated, are believed to be of value in maintaining the strength and nutrition of the patient, which are important considerations in speeding convalescence. Vitamin supplements are indicated only in those in whom previous malnutrition is suspected.

The return to activity should be gradual. A sustained drop in the serum bilirubin level with improvement in the cephalin flocculation reaction is usually a reliable indication to start the patient sitting up for a few minutes at a time, with the legs over the side of the bed. So long as brief periods of activity cause no excess sweating or exhaution they are not harmful and may be repeated. As improvement continues, a chair and slow ambulation are permitted. Patients with enlarged tender liver or marked prostration should proceed more cautiously, since relapses seem to occur more frequently in these groups. Strict bed rest until all tests and clinical features have become normal is not justified; indeed, return to full activity seems to be actually retarded in the overtreated case in some instances.

Many personal considerations enter into the management of convalescence. Obviously, patients who have sustained extensive hepatic damage, have suffered repeated relapses, or continue to show significant derangement in several of the standard liver function tests require a longer period to regain health. Much depends upon the effects of fatiguing experiences on the patient; if tolerance is low, it is better to alternate periods of activity with periods of reclining throughout the day, rather than enforcing overcautious immobilization or injudicious prodding. It is important for the patients to realize that, in spite of setbacks and periods of frustration, complete recovery is to be expected. The physician can unwittingly add greatly to their anxiety and introspection by exhibiting undue concern over a single, recalcitrantly abnormal laboratory finding or by repeating tests too frequently. On the other hand, he should maintain systematic evaluation of the hepatic status, regulate diet, assay the effects of resuming the use of alcohol, and direct the schedule of physical and mental activities and work load until complete recovery is assured. Decisions are especially difficult when subjective disabilities are not paralleled by demonstrable abnormalities in liver function. In most instances the convalescent should be given the benefit of the doubt and be treated with reassurance and patience.

Infectious hepatitis is notably transmissible in the incubation period to those in close contact with the patient and to those sharing toilet facilities. It is generally advisable to administer to these exposed individuals 1 to 3 cc. (0.04 to 0.06 cc. per kilogram of body weight) of immune serum globulin intramuscularly, as a prophylactic measure. All persons attending those with acute cases of hepatitis should observe strict cleanliness of the hands after contact with bedding and toilet articles. Strict syringe and needle sterilization should also be maintained.

Treatment of Hepatitis in Patients with Hepatic Insufficiency

Severe hepatic insufficiency is usually recognizable by rapidly deepening jaundice, strong fetor hepaticus, and mental disturbances consisting of increasing drowsiness, mental confusion, and coma. In some cases there may be wild delirium, negativism, and other personality changes, as well as flapping tremors and abnormal reflex reactions. A more serious manifestation is the development of a bleeding tendency with hemorrhages into the skin and from the nose, buccal mucosa, and gastrointestinal tract. Patients may manifest hepatic insufficiency early in the disease when parenchymal necrosis is extensive, or it may develop gradually as part of a progressive downhill course. It may appear suddenly with rapid shrinkage of the liver, especially in middle-aged females who previously had been running a satisfactory course. It develops not infrequently in patients with previous cirrhosis or chronic illness and may be precipitated by shock, hemorrhage, surgical procedure, or superimposed infection. Early recognition of hepatic insufficiency is of vital importance. The development of mental symptoms not attributable to drugs in a patient with hepatitis is to be regarded as a medical emergency, warranting prompt revision of routine management. It is recommended to withdraw all sedatives and medicaments containing ammonium salts or amino acids, discontinue or curtail drastically all protein feedings, and allow only liquid carbohydrates in sips by mouth, supplemented by almost continuous intravenous, slow-drip infusions of 10% dextrose in water. About three liters may be given during 24 hours. An important item in the treatment is the oral administration (by small stomach tube if necessary) of a broad-spectrum antibiotic such as chlortetracycline (Aureomycin) hydrochloride or chloramphenicol (Chloromycetin), 1 to 2 Gm. daily in divided doses. This medication decreases the production of ammonia within the intestine, depresses the production of endotoxins by the coliform organisms, and prevents phlegmonous infections of the alimentary canal, which are not uncommon in cases of advanced hepatic disease. The colon should be cleansed by a daily lavage with isotonic sodium chloride solution. A vitamin K preparation (menadiol sodium diphosphate), 20 to 40 mg., may be administered parenterally every second or third day, but massive daily doses are contraindicated. Other vitamins are not indicated in acute cases. These agents are probably ineffectually utilized by the failing liver and might conceivably give rise to abnormal metabolites.

If patients fail to improve on this regimen within 24 to 36 hours, if jaundice deepens, and if lethargy increases, adrenal steroid therapy with 200 mg. of cortisone (Cortisone, Cortogen, Cortone) acetate or 75 mg. of prednisone (Deltasone, Deltra, Meticorten) should be instituted in the hope that the inflammatory process within the liver may be lessened by the drug. It must be borne in mind, however, that glucocorticoids do not affect directly the viability of hepatic parenchyma in this disease and often are of no benefit.

It is obvious that the aforementioned regimen cannot be maintained longer than two weeks. The antibiotics eventually lose their inhibitory effects on the intestinal flora, and a strict carbohydrate diet is only an emergency measure. Electrolyte deficiencies may also develop. If there is clinical

improvement, gradual modification toward usual treatment should be instituted.

If the blood ammonia level is found to be significantly elevated, i.e., higher than 120 mg. per 100 ml. (Conway method), agents such as arginine hydrochloride given intravenously (25 Gm. in 500 cc. of 10% dextrose in water) or sodium glutamate also given intravenously (25 to 80 Gm. in 1,000 cc. of 10% dextrose in water) have been recommended to reduce the level of this cerebral intoxicant. It has been the experience of most observers, however, that high blood ammonia levels in hepatitis are but another indication of severe hepatic dysfunction, and it is doubtful if drugs that merely decrease these levels are important factors in the ultimate outcome.

It has long been known that patients with hepatic insufficiency who maintain a satisfactory urinary output have a more favorable prognosis than those with oliguria. It is therefore advisable, unless there is incontinence, to measure or estimate the daily fluid balance. A drop in blood pressure with suppression of urine may be benefited temporarily by the slow, intravenous administration of 100 to 200 cc. of salt-poor normal human serum albumin.

Careful conservation of the energy of the patient and gentle correction of disturbing details as they arise may prolong life until hepatic regeneration can take place. It is a sad commentary on present medical trends that as the patient becomes increasingly unable to tolerate therapeutic onslaughts, the physician, in his desperation, becomes increasingly aggressive in his ministrations!

Management of Protracted Hepatitis

Although the tendency in viral hepatitis is toward eventual healing, a certain number of patients run protracted courses or suffer a series of relapses. In this group are those who sustained massive initial parenchymal damage, those who continued exhausting activities during the acute phases of the disease, those infected by a particularly virulent virus, often acquired in foreign countries, and those with severe interstitial involvement as manifested by a large, firm liver and spleen, itching and features of cholangitic obstruction. Patients with associated debilitating diseases also tend to run a protracted course.

Protracted hepatitis may be relatively symptomless and is recognized only by the persistence, for six weeks or longer, of abnormal laboratory findings such as jaundice with a prompt direct reaction van den Bergh test, positive flocculation reactions, elevated serum alkaline phosphatase levels, and sulfobromophthalein (Bromsulfalein) retention exceeding 10% after 45 minutes. Not infrequently the liver remains enlarged and firm. In other instances, the patients may complain of lack of endurance, nervousness, depression, capricious appetite, indigestion, and flatulence. Periodic liver tenderness may be a disturbing symptom. Many of the abnormal tests and clinical features may be worsened by exhausting experiences. In severe cases, prostration is marked, even during strict bed rest.

The treatment of the protracted case of viral hepatitis with marked hepatic depletion consists primarily of maintaining nutrition in a weak, discouraged, dyspeptic individual. Frequent, small, tempting feedings are much better tolerated than large trays of food. The weak patient will drink when he will not chew, and the use of blendors and mixers in adding meats, milk powder, and flavors to eggnogs will add to the variety of the diet. Vitamin supplements in moderation are indicated in most cases. Visits from relatives and friends must be curtailed, and physical and mental challenges regulated to conform with the vacillations of the clinical course. Maintaining a spirit of optimism and hope in the sick room is a most important consideration. The course may be tedious and remittent, even in patients who, after months and years, make a satisfactory recovery. Often there is residual scar tissue in the liver, but the inflammatory process will eventually subside.

Adrenal steroid therapy has been found useful in the treatment of certain cases of protracted hepatitis, especially those of the cholangiolitic type. It may also prove beneficial in patients who suffer repeated relapses or those who show little clinical improvement and unchanging abnormal laboratory findings after six weeks or longer under optimal conservative management. In some instances a favorable response is prompt and dramatic, and improvement will continue spontaneously after but a few days of glucocorticoid therapy (5 to 50 mg. of prednisone daily) for weeks or months with gradual reduction of dosage. Glucocorticoid therapy with cortisone or its derivatives is not indicated, however, in patients manifesting spontaneous improvement or those without symptoms who show a single abnormality such as jaundice with a delayed, indirect van den Bergh test, or a persistingly positive cephalin flocculation reaction, or thymol turbidity.

Management of Chronic Progressive Hepatitis

In rare instances viral hepatitis develops into a chronic progressive disease with continuing break-down of parenchymal cells, scar formation, and increasing distortion of the vasculature of the liver. The condition is characterized by such features as a large, hard, irregular liver, splenomegaly, portal hypertension, intermittent jaundice with a prompt direct reaction van den Bergh test, spider angiomas of the skin, and hyperglobulinemia. The majority of patients run a progressive downhill course, despite all forms of therapy. However, there are marked variations in the severity of the process. A few patients will be encountered who remain relatively symptom-free while on therapy with 20 to 70 mg. of cortisone daily but who develop jaundice, abnormal function tests, and histological evidence of hepatic inflammation whenever the therapy is discontinued or the dosage decreased below required maintenance levels. In other patients the severity of the process seems ameliorated by steroids but manifestations of hepatic deterioration continue, whereas others derive no demonstrable benefit from this form of medication. The prevailing opinion at present is that all patients with demonstrable chronic hepatitis should be given a test therapeutic trial with steroids, preferably prednisone because of its lesser sodium-retaining action. Should bleeding from esophageal varices develop, a shunting procedure of the portal vein to the vena cava should be performed as soon as the patient can be conditioned for a major operation. Portal hypertension in this type of liver disease always increases, and fatal bleeding can be anticipated as a certainty unless corrected by surgery. Chronic hepatitis after viral infection is not caused or aggravated by specific dietary deficiencies. Although an adequate food intake is to be commended, the present overemphasis of the need for foods high in proteins, vitamin supplements, and lipotropic agents such as choline or methionine is not supported by critical clinical trials.

Conclusions

Viral hepatitis varies widely in symptomatology and chronicity. The average case requires little special therapy beyond the avoidance of exhausting activity. Hepatic insufficiency is a clinical emergency requiring special management. Protracted and chronic cases are often benefited by adrenal steroid therapy.

J.A.M.A. *165*:1696 (Nov. 30) 1957.

► *The Fourth Supplement to the Directory* of Membership of Rho Chi Society, including members from July 1, 1956 to June 30, 1957, has just been issued by Dr. Edward J. Rowe, Secretary-Treasurer of Rho Chi who is associated with the College of Pharmacy, Butler University, Indianapolis.

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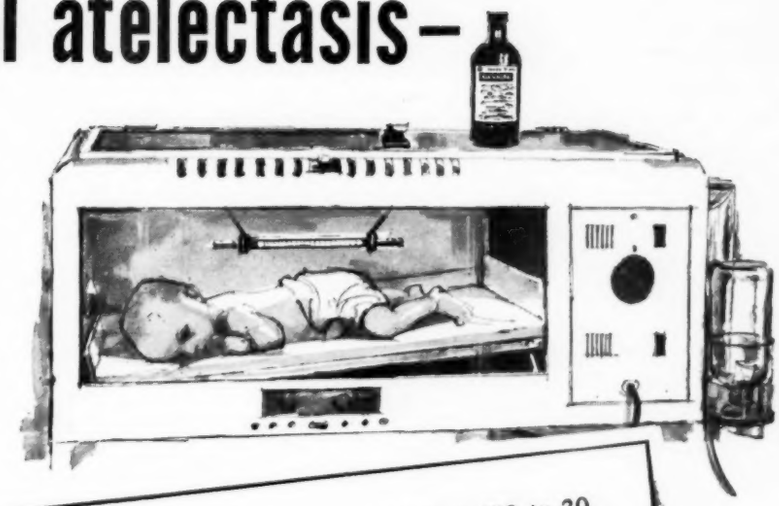
in neonatal atelectasis—

*". . . results are impressive. This dreaded condition usually improved in a few hours, and it was really striking to see a cyanotic baby with gasping respirations and suprasternal retraction become relaxed and pink in such a short period of time."**



CASE REPORT

A typical Alevaire case history—D., a premature male infant (28 to 30 weeks) was delivered as a frank breech. Weight was 3 lb., 6 oz. After birth the patient's condition was poor; shallow, irregular respiration, suprasternal retraction, gasping and cyanosis were present. Breath sounds were diminished, and bilateral atelectatic rales were observed.

The infant was placed in an optimal oxygen concentration in an incubator. Although color and respiration somewhat improved, he remained lethargic. His condition became worse the following day, and respirations were rapid and shallow.

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The next day, the lungs were almost clear on auscultation and no respiratory distress was noted. Therapy was discontinued on the third day; the patient was discharged six weeks later weighing 5 lb., 7 oz.

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- pneumoconiosis • smoke, kerosene poisoning
- poliomyelitis (respiratory complications)
- routine oxygen therapy • tracheotomy
- prevention of postoperative pulmonary complications

*Smessaert, Andre; Collins, V. J.; and Kracum, V. D.: *New York Jour. Med.*, 55:1587, June 1, 1955.

Alevaire, trademark reg. U.S. Pat. Off.

Reactions to Antibiotics

Severe Reactions to antibiotics were discussed by Welch, Lewis, Weinstein, and Staffa of the Food and Drug Administration at the recent Antibiotic Conference held in Washington, D. C. During the past few years it has become evident that the extensive and sometimes indiscriminate use of antibiotics has resulted in an increase in the incidence of reactions to these drugs. In a sampling survey made in 10 large cities in 1953 a total of 88 anaphylactoid reactions were encountered, of which all but four followed administration of penicillin preparations. A total of 95 hospitals with a capacity of 5,100 beds were surveyed and, since severe reactions may occur in a physician's office or elsewhere without the patient being admitted to a hospital, reports of cases were also obtained from medical examiners, pathologists, allergists, internists, and other physicians.

The present survey was much more extensive than the previous one, covering the years from 1953 to date. Every State in the Union and the District of Columbia were included in the survey. Of the 5,431 general hospitals in the United States with a total bed capacity of 685,655, eight hundred twenty-seven hospitals having a bed capacity of 198,332 were covered. In addition, 1,637 physicians were interviewed. These represented a cross section of medical practitioners in each geographical area and included general practitioners (urban and rural), allergists, dermatologists, hematologists, surgeons, and internists.

A total of 3,419 case histories of reactions to antibiotics were reported and evaluated in the survey. Of these, 422 were discarded because of insufficient data to classify, or because antibiotics were not involved, or because they occurred outside the period covered by the survey. A total of 1,072 reactions were classified as severe (life threatening) and these included 809 with anaphylactoid shock, 107 superinfections, 70 severe skin reactions, 46 blood dyscrasias, and 38 cases of angioneurotic edema with cerebral or respiratory involvement. A total of 1,925 were classified as non-life threatening cases. A breakdown of the kinds of blood dyscrasias, age groups and sex affected, geographic distortion of cases, and the antibiotics involved was discussed. The preponderance of reactions followed administration of penicillin.

Barnstead Briefs

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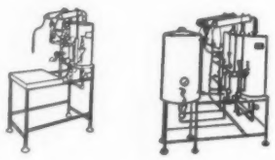

KEEPING DISTILLED WATER PURE

Contamination of distilled water often occurs through improper handling and unclean receptacles after it is received from the still. Thus the purity required for many exacting hospital requirements is ruined. An easy check for such contamination is by a conductivity type test

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OPERATING AND MAINTENANCE HINTS

Many Hospital Technicians are concerned with the pH of distilled water. When exposed to air, distilled water will absorb the CO_2 in the atmosphere causing a decrease in its pH (increased acidity). This can be guarded against by using only freshly distilled water. If the freshly distilled water itself has a low pH, it can be increased by turning down the cooling water valve of the still. The condenser, operating at a higher heat, will drive off the CO_2 and effect an increase in pH.

FIELD REPORTS

The purification of water by demineralization (ion exchange) is generally far less expensive than by distillation, though bacteria, organics, and pyrogens are not removed by this process. Some hospitals use Barnstead Demineralizers to provide pure water for washing glassware etc., thus effecting operating savings where sterility and freedom of pyrogens is not important. Hospitals also use demineralizers to purify water before it is fed to the evaporator . . . an effective safeguard against foaming and priming.

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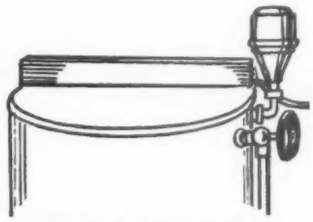
80 years ago when Barnstead was first founded, distilled water was used rarely in the hospital. One use was for drinking purposes as part of a diet routine. It is of interest that Alexander Graham Bell, inventor of the telephone, ascribed his good health and 75 years of age to "a small distiller (Barnstead) from which I procure all my drinking water".



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POSITIONS

in hospital pharmacy

PERSONNEL PLACEMENT SERVICE

The Personnel Placement Service is operated without charge for the benefit of hospitals and pharmacist members of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. The ultimate purpose is the improvement of pharmaceutical services in hospitals, by more adequately fulfilling hospital pharmacy personnel needs and by locating positions which provide challenging opportunities for pharmacists who have indicated an interest in a hospital career.

By participating in the service, the hospital indicates a desire to achieve a pharmaceutical service which meets the *Minimum Standard for Pharmacies in Hospitals.* A description of the position should be submitted to the Division of Hospital Pharmacy on the forms provided. The hospital will receive applications directly from the applicant. The hospital agrees to reply to each application received and to notify the Division of Hospital Pharmacy when the position is filled.

The pharmacist, by participating, agrees to submit a Personnel Placement Service Information Form to the Division of Hospital Pharmacy. The applicant will then be notified of openings listed with the Service as they become available and can negotiate directly with the hospital if he is interested. It is agreed that the Division of Hospital Pharmacy will be notified as soon as a position is accepted.

A listing of positions open and wanted will be made regularly in the AMERICAN JOURNAL OF HOSPITAL PHARMACY without charge. Neither the name of the hospital offering the position nor the name of the applicant will be listed, except by code. All inquiries should be directed as shown above, including the code number.

Address all inquiries to

Division of Hospital Pharmacy
2215 Constitution Avenue, N. W.
Washington, 7, D. C.

positions wanted

CHIEF PHARMACIST—prefer small general hospital, but will consider larger hospital; prefer Michigan, but will consider remainder of Midwest. Two years' experience in hospital pharmacy. PW-10.

PHARMACIST—female; experienced in both hospital and retail pharmacy. Prefer southwest or mid-Atlantic area. PW-11.

CHIEF PHARMACIST—prefer general hospital in Florida; registered in Ohio and Florida; experienced in both hospital and retail pharmacy. PW-12.

CHIEF PHARMACIST—or assistant chief pharmacist at large hospital; prefer St. Louis vicinity; presently employed as staff pharmacist in hospital; registered in Missouri. PW-13.

CHIEF PHARMACIST—prefer Minnesota or California, with registration in those states; ten years' experience with government service, including commissions in U. S. Public Health Service and in the Navy; experience with the Veterans' Administration as Chief Pharmacist; Pharm. D. degree. PW-15.

PHARMACIST—New Jersey registration; prefer Pennsylvania, Florida, D. C., or Virginia; experienced in managing retail pharmacy. PW-18.

CHIEF PHARMACIST—OR CHIEF PHARMACIST-PURCHASING AGENT; prefer non-sectarian and non-governmental institution of 200-bed capacity or larger; experienced in managing retail and hospital pharmacy. PW-19.

PHARMACIST—registered in Illinois and Missouri; six years' experience in hospital pharmacy; desires immediate location. PW-20.

CHIEF PHARMACIST IN TEACHING HOSPITAL—registered in Indiana, Michigan and Missouri; prefer general hospital in Midwest; experienced in teaching and in hospital pharmacy. PW-26.

STAFF PHARMACIST—prefer Chicago vicinity; registered in Illinois; graduate of the University of Illinois, College of Pharmacy. PW-31.

CHIEF PHARMACIST—or assistant chief pharmacist in medium size hospital; registered in Indiana, Michigan, and Wisconsin; six years' experience as chief pharmacist; experienced as pharmacist-purchasing agent, two years; prefer Midwest or East. PW-32.

STAFF PHARMACIST—graduate, Massachusetts College of Pharmacy; age, 27; registered in Massachusetts and New Hampshire; four years' experience before registration and four years in store with large prescription volume. PW-35.

CHIEF PHARMACIST—or assistant chief pharmacist; M. S. in hospital pharmacy with internship; available after February, 1958. P.W-36.

STAFF PHARMACIST—graduate of Howard University, 1957; age 24; male; D. C. registration. PW-43.

PHARMACIST—graduate of Medical College of Virginia; age 26; served two years in Marine Corps; managerial experience. PW-45.

HOSPITAL PHARMACY INTERN—graduate of the University of Washington College of Pharmacy; age 25; presently completing military requirements; prefer Northwest. PW-46.

PHARMACIST—graduate of Wayne University College of Pharmacy; hospital experience; prefer D. C. area. PW-49.

STAFF PHARMACIST—graduate Howard University College of Pharmacy in 1957; age 31; limited experience but anxious to learn; any location. PW-50.

STAFF PHARMACIST—or assistant chief pharmacist; graduate George Washington University College of Pharmacy; prefer D. C. or Florida area; registered in D.C. PW-52.

PHARMACIST—graduate State University of Iowa College of Pharmacy; some hospital pharmacy experience; extensive managerial experience; registered in Illinois and Iowa. PW-53.

CHIEF PHARMACIST—300 plus bed hospital preferred; completed hospital pharmacy internship at Jefferson Medical College Hospital; registered in Pennsylvania and Texas; age 25; male; completed service requirements. PW-55.

STAFF PHARMACIST—desires position in Eastern Pennsylvania; graduate of Philadelphia College of Pharmacy; two years' graduate study at Northwestern University; three years' experience at University of Chicago Clinics; single; male. PW-57.

CHIEF PHARMACIST—in small hospital, or assistant chief pharmacist or staff pharmacist in large hospital; Southwest preferred; graduate of Southwestern State College, School of Pharmacy; hospital pharmacy internship at Springfield City Hospital, Springfield, Ohio; registered in Oklahoma. PW-58.

CHIEF PHARMACIST—any location; M. S. degree in hospital pharmacy from the University of Michigan; completed service requirements; single, male, age 29. PW-59.

CHIEF PHARMACIST—prefer middle-West; registered in Illinois; female, single; graduate of University of Illinois College of Pharmacy; presently employed as chief pharmacist. PW-61.

CHIEF PHARMACIST—M. S. Degree in hospital pharmacy; prefer East; male, single; extensive experience, including pharmacy and administrative officer in Air Force. PW-62.

STAFF PHARMACIST—completed military requirements; experienced in hospital pharmacy; prefer mid-Atlantic area; single, male. PW-63.

positions open

STAFF PHARMACIST—registered in Illinois; for manufacturing or dispensing in large teaching hospital; excellent equipment; good hours; two weeks vacation; sick leave; minimum starting salary, $470.00 per month; higher salary for those experienced in manufacturing. PO-1.

CHIEF PHARMACIST—650 bed hospital, the largest voluntary hospital specializing in the treatment of long-term illness; a growing institution presenting a major challenge to a pharmacist interested in both administration and pharmacology. PO-2.

STAFF PHARMACIST—132 bed hospital; salary open; hospital experienced preferred. PO-4.

ASSISTANT CHIEF PHARMACIST—eligible for licensure in New Jersey; 350-bed hospital. PO-6.

PHARMACIST—80 bed hospital; full responsibility for pharmacy and central sterile supply services; minimum of one year experience in hospital pharmacy; salary open. PO-17.

ASSISTANT CHIEF PHARMACIST—209 bed general hospital, expanding to 300 beds; 40-hour week; three weeks' vacation; $5,000.00 annually; New Jersey registration required. PO-18.

PHARMACIST—162 bed hospital located in Ohio; assume complete charge of the department; prefer woman with hospital internship; salary open. PO-21.

ASSISTANT CHIEF PHARMACIST—185-bed hospital; prefer member of Seventh Day Adventist Church. PO-22.

CHIEF PHARMACIST—Kentucky registration required; salary, $6,420; 40-hour week; 4 week vacation; non-contributory retirement plan; guaranteed annual salary increases. PO-26.

STAFF PHARMACIST—female preferred; 274 bed general hospital and 172 bed maternity hospital; California registration required; salary, $525.00 per month; benefit program represents 17 percent of base salary. PO-27.

ASSISTANT CHIEF PHARMACIST AND STAFF PHARMACIST—550 bed general hospital in South Carolina; hospital experience preferred; salary open; 44 hour week; two week vacation. PO-29.

DIRECTOR OF PHARMACY—605 bed hospital located in the East; plan, organize and direct complete pharmaceutical service for this teaching hospital; salary, $6,000 to $7,200 per year. PO-30.

ASSISTANT CHIEF PHARMACIST—315 bed community hospital located in New York state; female preferred; 40 hours per week; three weeks' vacation. Salary open. PO-31.

ASSISTANT CHIEF PHARMACIST—181 bed general hospital; California registration required; 40 hour week; two weeks vacation; salary $450 to $500 per month. PO-32

ASSISTANT CHIEF PHARMACIST AND STAFF PHARMACIST—600 bed hospital located in Washington state; assistant chief pharmacist to have M. S. in hospital pharmacy and/or internship in hospital pharmacy; staff pharmacist to have B. S. in pharmacy; 44 hour week; two weeks vacation; salary open. PO-33.

STAFF PHARMACIST—550 bed general hospital located in Ohio; registration required; 40 hour week; two weeks' vacation; salary $2.50 per hour or based on experience. PO-34.

STAFF PHARMACIST—259 bed general hospital; Virginia registration required; hospital pharmacy experience preferred; 40 hour week, 2 weeks vacation; salary open. PO-35.

STAFF PHARMACIST—750 bed general hospital located in New York state; B. S. degree required; hospital pharmacy experience desirable but not necessary; 40 hour week; two weeks vacation; $415.00 per month. PO-36.

STAFF PHARMACIST—manufacturing, dispensing, inventory control and some supervision; registration in Tennessee required; salary, $385.00 to $440.00 per month; 44 hour week; paid sick leave. PO-37.

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